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UTILITY PATENT APPLICATION TRANSMITTAL <small>(Only for new nonprovisional applications under 37 CFR 1.53(b))</small>		Attorney Docket No. DM-6864-A First Named Inventor or Application Identifier HE et al. Express Mail Label No. EI792013109
APPLICATION ELEMENTS <i>See MPEP chapter 600 concerning utility patent application contents.</i>		Assistant Commissioner for ADDRESS TO: Patents Box Patent Application Washington, DC 20231
1. <input checked="" type="checkbox"/> Fee (Authority to charge deposit account below.) <small>(submit on original, and a duplicate for fee processing)</small>		6. <input type="checkbox"/> Microfiche Computer Program (Appendix)
2. <input checked="" type="checkbox"/> Specification [Total Pages 318] <small>(preferred arrangement set forth below)</small> <ul style="list-style-type: none"> - Descriptive title of the invention - Cross References to Related Applications (if needed) - Statement Regarding Fed sponsored R&D (if needed) - Reference to Microfiche Appendix (if filed) - Background of the Invention - Brief Summary of the Invention - Brief Description of the Drawings (if filed) - Detailed Description - Claim(s) - Abstract of the Disclosure 		7. Nucleotide and/or Amino Acid Sequences Submission <small>(if applicable, all necessary)</small> <ul style="list-style-type: none"> a. <input type="checkbox"/> Computer Readable Copy b. <input type="checkbox"/> Paper Copy (identical to computer copy) c. <input type="checkbox"/> Statement verifying identity of above copies
ACCOMPANYING APPLICATION PARTS		
8. <input type="checkbox"/> Power of Attorney 9. <input type="checkbox"/> Information Disclosure Statement (IDS)/Cover Letter plus PTO-1449 <input type="checkbox"/> Copies of IDS Citations 10. <input type="checkbox"/> Preliminary Amendment 11. <input checked="" type="checkbox"/> Return Receipt Postcard (MPEP 503) <small>(Should be specifically itemized)</small> 12. <input type="checkbox"/> Certified Copy of Priority Document(s) <small>(if foreign priority is claimed)</small> 13. <input type="checkbox"/> Other		
14. If a CONTINUATION APPLICATION, check appropriate box and supply the requisite information: <input type="checkbox"/> Continuation <input type="checkbox"/> Divisional <input checked="" type="checkbox"/> Continuation-in-part(CIP) of prior application No.: 08/899,242		
DELETION OF INVENTOR(S) STATEMENT		
15. This application is being filed by less than all the inventors named in the prior application. In accordance with 37 CFR 1.63(d)(2) and 1.33(b), the Assistant Commissioner is requested to delete the name(s) of the following person who are not inventors of the invention being claimed in this application:		
16. <input checked="" type="checkbox"/> Amend the specification by inserting before the first line the sentence: -- This is a <input checked="" type="checkbox"/> continuation-in-part, <input type="checkbox"/> continuation, <input type="checkbox"/> division of application No. 08/899,242 filed July 23, 1997.		
17. <input type="checkbox"/> Priority of foreign application No. _____ filed on _____ in _____ _____ is claimed under 35 U.S.C. 119. (country)		

CLAIMS	(1) FOR	(2) NUMBER FIELD	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
	TOTAL CLAIMS (37 CFR 1.16(b))	42 - 20 =	22	22 x \$ 22 =	484.
	INDEPENDENT CLAIMS (37 CFR 1.16(b))	3 - 3 =	0	x \$ 80 =	—
	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$ 260 =	260
				BASIC FEE (37 CFR 1.16(a))	+ \$ 770.00
				Total =	1514.00\$
18.	The Commissioner is hereby authorized to credit any overpayments or charge the following fees to Deposit Account No. <u>04-1928</u> :				
a.	<input checked="" type="checkbox"/>	Fees required under 37 CFR 1.16			
b.	<input type="checkbox"/>	Fees required under 37 CFR 1.17.			
19.	<input type="checkbox"/>	Other:			

20. CORRESPONDENCE ADDRESS					
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21. SIGNATURE OF ATTORNEY OR AGENT REQUIRED		
NAME	MAUREEN P. O'BRIEN	REG. NO.
SIGNATURE	<i>Maureen P. O'Brien</i>	P-42,043
DATE	<i>January 28, 1998</i>	

TITLE

AZOLO TRIAZINES AND PYRIMIDINES

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FIELD OF THE INVENTION

This invention relates a treatment of psychiatric disorders and neurological diseases including major depression, anxiety-related disorders, 10 post-traumatic stress disorder, supranuclear palsy and feeding disorders as well as treatment of immunological, cardiovascular or heart-related diseases and colonic hypersensitivity associated with psychopathological disturbance and stress, by 15 administration of certain [1,5-a]-pyrazolo-1,3,5-triazines, [1,5-a]-1,2,3-triazolo-1,3,5-triazines, [1,5-a]-pyrazolo-pyrimidines and [1,5-a]-1,2,3-triazolo-pyrimidines.

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BACKGROUND OF THE INVENTION

Corticotropin releasing factor (herein referred to as CRF), a 41 amino acid peptide, is the primary physiological regulator of proopiomelanocortin (POMC) - derived peptide secretion from the anterior pituitary gland [J. Rivier et al., *Proc. Nat. Acad. Sci. (USA)* 80:4851 (1983); W. Vale et al., *Science* 213:1394 (1981)]. In addition to its endocrine role at the pituitary gland, immunohistochemical localization of CRF has demonstrated that the hormone has a broad 25 extrahypothalamic distribution in the central nervous system and produces a wide spectrum of autonomic, electrophysiological and behavioral effects consistent with a neurotransmitter or neuromodulator role in brain [W. Vale et al., *Rec. Prog. Horm. Res.* 39:245 (1983); G.F. Koob, *Persp. Behav. Med.* 2:39 (1985); 30 E.B. De Souza et al., *J. Neurosci.* 5:3189 (1985)].

There is also evidence that CRF plays a significant role in integrating the response of the immune system to physiological, psychological, and immunological stressors [J.E. Blalock, *Physiological Reviews* 69:1 5 (1989); J.E. Morley, *Life Sci.* 41:527 (1987)].

Clinical data provide evidence that CRF has a role in psychiatric disorders and neurological diseases including depression, anxiety-related disorders and feeding disorders. A role for CRF has 10 also been postulated in the etiology and pathophysiology of Alzheimer's disease, Parkinson's disease, Huntington's disease, progressive supranuclear palsy and amyotrophic lateral sclerosis as they relate to the dysfunction of CRF neurons in 15 the central nervous system [for review see E.B. De Souza, *Hosp. Practice* 23:59 (1988)].

In affective disorder, or major depression, the concentration of CRF is significantly increased in the cerebral spinal fluid (CSF) of drug-free individuals 20 [C.B. Nemeroff et al., *Science* 226:1342 (1984); C.M. Banki et al., *Am. J. Psychiatry* 144:873 (1987); R.D. France et al., *Biol. Psychiatry* 28:86 (1988); M. Arato et al., *Biol Psychiatry* 25:355 (1989)]. Furthermore, the density of CRF receptors is 25 significantly decreased in the frontal cortex of suicide victims, consistent with a hypersecretion of CRF [C.B. Nemeroff et al., *Arch. Gen. Psychiatry* 45:577 (1988)]. In addition, there is a blunted adrenocorticotropic (ACTH) response to CRF (i.v. 30 administered) observed in depressed patients [P.W. Gold et al., *Am J. Psychiatry* 141:619 (1984); F. Holsboer et al., *Psychoneuroendocrinology* 9:147 (1984); P.W. Gold et al., *New Eng. J. Med.* 314:1129 (1986)]. Preclinical studies in rats and non-human 35 primates provide additional support for the hypothesis that hypersecretion of CRF may be involved in the

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symptoms seen in human depression [R.M. Sapolsky, *Arch. Gen. Psychiatry* 46:1047 (1989)]. There is preliminary evidence that tricyclic antidepressants can alter CRF levels and thus modulate the numbers of 5 CRF receptors in brain [Grigoriadis et al., *Neuropsychopharmacology* 2:53 (1989)].

There has also been a role postulated for CRF in the etiology of anxiety-related disorders. CRF produces anxiogenic effects in animals and 10 interactions between benzodiazepine / non-benzodiazepine anxiolytics and CRF have been demonstrated in a variety of behavioral anxiety models [D.R. Britton et al., *Life Sci.* 31:363 (1982); C.W. Berridge and A.J. Dunn *Regul. Peptides* 16:83 (1986)]. 15 Preliminary studies using the putative CRF receptor antagonist a-helical ovine CRF (9-41) in a variety of behavioral paradigms demonstrate that the antagonist produces "anxiolytic-like" effects that are qualitatively similar to the benzodiazepines [C.W. Berridge and A.J. Dunn *Horm. Behav.* 21:393 (1987), *Brain Research Reviews* 15:71 (1990)]. Neurochemical, endocrine and receptor binding studies have all demonstrated interactions between CRF and benzodiazepine anxiolytics providing further evidence 20 for the involvement of CRF in these disorders. Chlordiazepoxide attenuates the "anxiogenic" effects of CRF in both the conflict test [K.T. Britton et al., *Psychopharmacology* 86:170 (1985); K.T. Britton et al., *Psychopharmacology* 94:306 (1988)] and in the 25 acoustic startle test [N.R. Swerdlow et al., *Psychopharmacology* 88:147 (1986)] in rats. The benzodiazepine receptor antagonist (Ro15-1788), which was without behavioral activity alone in the operant conflict test, reversed the effects of CRF in a dose- 30 dependent manner while the benzodiazepine inverse 35

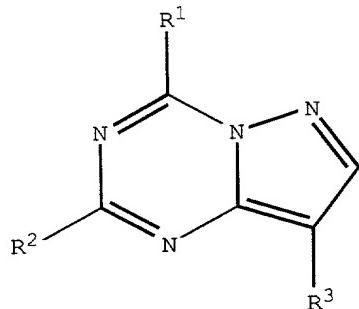
agonist (FG7142) enhanced the actions of CRF [K.T. Britton et al., *Psychopharmacology* 94:306 (1988)].

The mechanisms and sites of action through which the standard anxiolytics and antidepressants produce their therapeutic effects remain to be elucidated. It has been hypothesized however, that they are involved in the suppression of the CRF hypersecretion that is observed in these disorders. Of particular interest is that preliminary studies examining the effects of a CRF receptor antagonist (α -helical CRF9-41) in a variety of behavioral paradigms have demonstrated that the CRF antagonist produces "anxiolytic-like" effects qualitatively similar to the benzodiazepines [for review see G.F. Koob and K.T. Britton, In: *Corticotropin-Releasing Factor: Basic and Clinical Studies of a Neuropeptide*, E.B. De Souza and C.B. Nemeroff eds., CRC Press p221 (1990)].

Several publications describe corticotropin releasing factor antagonist compounds and their use to treat psychiatric disorders and neurological diseases. Examples of such publications include DuPont Merck PCT application US94/11050, Pfizer WO 95/33750, Pfizer WO 95/34563, Pfizer WO 95/33727 and Pfizer EP 0778 277 A1.

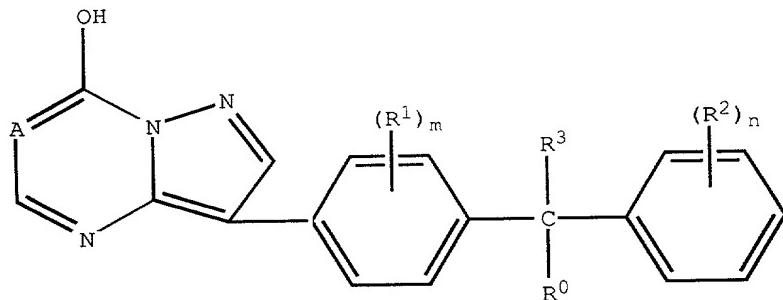
Insofar as is known, [1,5-a]-pyrazolo-1,3,5-triazines, [1,5-a]-1,2,3-triazolo-1,3,5-triazines, [1,5-a]-pyrazolo-pyrimidines and [1,5-a]-1,2,3-triazolo-pyrimidines, have not been previously reported as corticotropin releasing factor antagonist compounds useful in the treatment of psychiatric disorders and neurological diseases. However, there have been publications which teach some of these compounds for other uses.

For instance, EP 0 269 859 (Ostuka, 1988) discloses pyrazolotriazine compounds of the formula



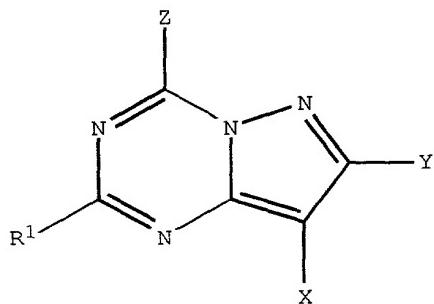
- where R^1 is OH or alkanoyl, R^2 is H, OH, or SH, and R^3 is an unsaturated heterocyclic group, naphthyl or
 5 substituted phenyl, and states that the compounds have xanthine oxidase inhibitory activity and are useful for treatment of gout.

EP 0 594 149 (Ostuka, 1994) discloses
 10 pyrazolotriazine and pyrazolopyrimidine compounds of the formula



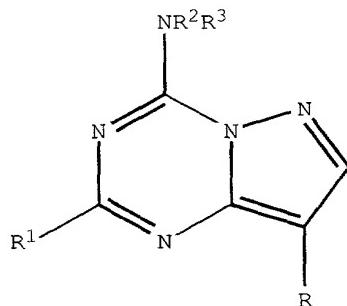
- 15 where A is CH or N, R^0 and R^3 are H or alkyl, and R^1 and R^2 are H, alkyl, alkoxy, alkylthio, nitro, etc., and states that the compounds inhibit androgen and are useful in treatment of benign prostatic hypertrophy and prostatic carcinoma.

20 US 3,910,907 (ICI, 1975) discloses pyrazolotriazines of the formula:



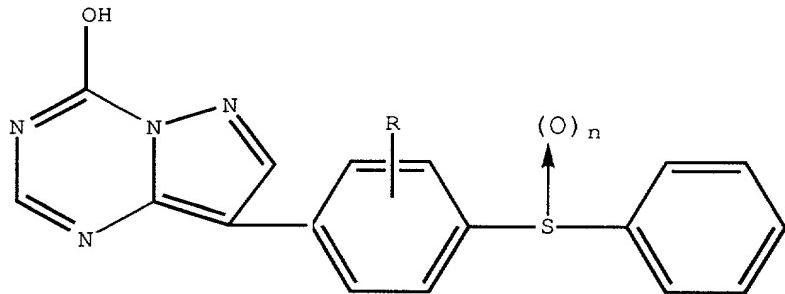
where R¹ is CH₃, C₂H₅ or C₆H₅, X is H, C₆H₅, m-CH₃C₆H₄, CN, COOEt, Cl, I or Br, Y is H, C₆H₅, o-CH₃C₆H₄, or p-CH₃C₆H₄, and Z is OH, H, CH₃, C₂H₅, C₆H₅, n-C₃H₇, i-C₃H₇, SH, SCH₃, NHC₄H₉, or N(C₂H₅)₂, and states that the compounds are c-AMP phosphodiesterase inhibitors useful as bronchodilators.

10 US 3,995,039 discloses pyrazolotriazines of the formula:



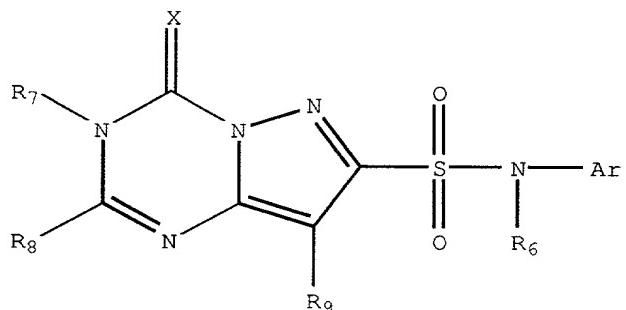
15 where R¹ is H or alkyl, R² is H or alkyl, R³ is H, alkyl, alkanoyl, carbamoyl, or lower alkylcarbamoyl, and R is pyridyl, pyrimidinyl, or pyrazinyl, and states that the compounds are useful as bronchodilators.

20 US 5,137,887 discloses pyrazolotriazines of the formula



where R is lower alkoxy, and teaches that the compounds
are xanthine oxidase inhibitors and are useful for
5 treatment of gout.

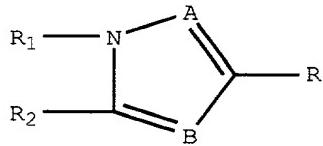
US 4,892,576 discloses pyrazolotriazines of the formula



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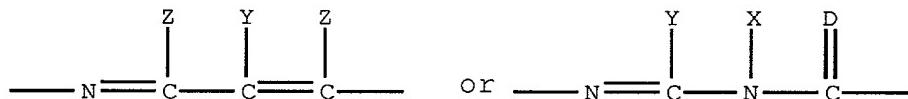
where X is O or S, Ar is a phenyl, naphthyl, pyridyl or thiienyl group, R6-R8 are H, alkyl, etc., and R9 is H, alkyl, phenyl, etc. The patent states that the
15 compounds are useful as herbicides and plant growth regulators.

US 5,484,760 and WO 92/10098 discloses
herbicidal compositions containing, among other things,
20 a herbicidal compound of the formula



where A can be N, B can be CR₃, R₃ can be phenyl or substituted phenyl, etc., R is -N(R₄)SO₂R₅ or -SO₂N(R₆)R₇

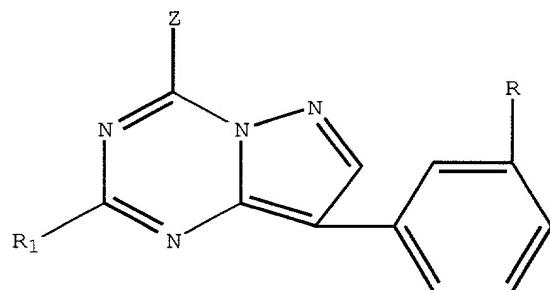
5 and R₁ and R₂ can be taken together to form



where X, Y and Z are H, alkyl, acyl, etc. and D is O or
10 S.

US 3,910,907 and Senga et al., J. Med. Chem., 1982, 25, 243-249, disclose triazolotriazines cAMP phosphodiesterase inhibitors of the formula

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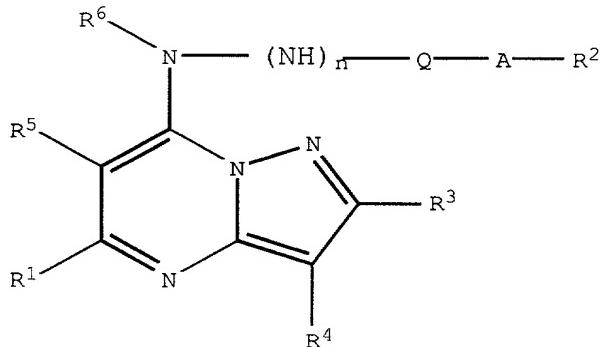


where Z is H, OH, CH₃, C₂H₅, C₆H₅, n-C₃H₇, iso-C₃H₇, SH, SCH₃, NH(n-C₄H₉), or N(C₂H₅)₂, R is H or CH₃, and R₁ is
20 CH₃ or C₂H₅. The reference lists eight therapeutic areas where inhibitors of cAMP phosphodiesterase could have utility: asthma, diabetes mellitus, female fertility control, male infertility, psoriasis, thrombosis, anxiety, and hypertension.

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WO95/35298 (Otsuka, 1995) discloses pyrazolopyrimidines and states that they are useful as analgesics. The compounds are represented by the formula

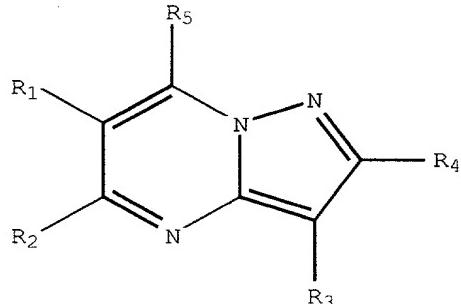
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where Q is carbonyl or sulfonyl, n is 0 or 1, A is a single bond, alkylene or alkenylene, R¹ is H, alkyl, etc., R² is naphthyl, cycloalkyl, heteroaryl, substituted phenyl or phenoxy, R³ is H, alkyl or phenyl, R⁴ is H, alkyl, alkoxycarbonyl, phenylalkyl, optionally phenylthio-substituted phenyl, or halogen, R⁵ and R⁶ are H or alkyl.

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EP 0 591 528 (Otsuka, 1991) discloses anti-inflammatory use of pyrazolopyrimidines represented by the formula

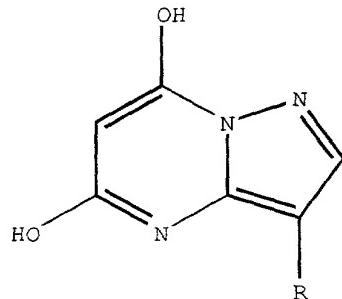


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where R₁, R₂, R₃ and R₄ are H, carboxyl, alkoxycarbonyl, optionally substituted alkyl, cycloalkyl, or phenyl, R₅

is SR₆ or NR₇R₈, R₆ is pyridyl or optionally substituted phenyl, and R₇ and R₈ are H or optionally substituted phenyl.

- 5 Springer et al, J. Med. Chem., 1976, vol. 19, no. 2, 291-296 and Springer U.S. patents 4021,556 and 3,920,652 disclose pyrazolopyrimidines of the formula

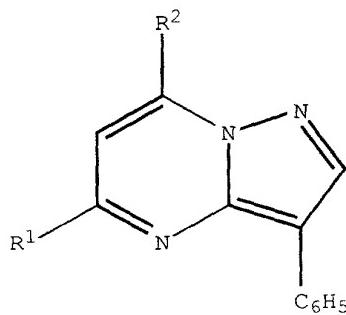


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where R can be phenyl, substituted phenyl or pyridyl, and their use to treat gout, based on their ability to inhibit xanthine oxidase.

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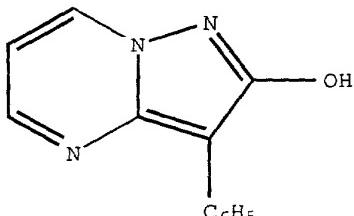
Joshi et al., J. Prakt. Chemie, 321, 2, 1979, 341-344, discloses compounds of the formula



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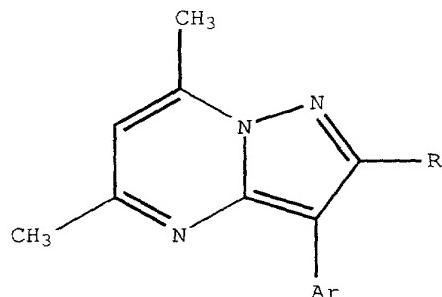
where R¹ is CF₃, C₂F₅, or C₆H₄F, and R² is CH₃, C₂H₅, CF₃, or C₆H₄F.

Maquestiau et al., Bull. Soc. Belg., vol.101, no. 2, 1992, pages 131-136 discloses a pyrazolo[1,5-a]pyrimidine of the formula



Ibrahim et al., Arch. Pharm. (weinheim) 320, 487-491 (1987) discloses pyrazolo[1,5-a]pyrimidines of the formula

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where R is NH₂ or OH and Ar is 4-phenyl-3-cyano-2-aminopyrid-2-yl.

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Other references which disclose azolopyrimidines included EP 0 511 528 (Otsuka, 1992), US 4,997,940 (Dow, 1991), EP 0 374 448 (Nissan, 1990), US 4,621,556 (ICN, 1997), EP 0 531 901 (Fujisawa, 1993), US 4,567,263 (BASF, 1986), EP 0 662 477 (Isagro, 1995), DE 4 243 279 (Bayer, 1994), US 5,397,774 (Upjohn, 1995), EP 0 521 622 (Upjohn, 1993), WO 94/109017 (Upjohn, 1994), J. Med. Chem., 24, 610-613 (1981), and J. Het. Chem., 22, 601 (1985).

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SUMMARY OF THE INVENTION

In accordance with one aspect, the present invention provides novel compounds, pharmaceutical compositions and methods which may be used in the treatment of affective disorder, anxiety, depression, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal disease, anorexia nervosa or other feeding disorder, drug or alcohol withdrawal symptoms, drug addiction, inflammatory disorder, fertility problems, disorders, the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, or a disorder selected from inflammatory disorders such as rheumatoid arthritis and osteoarthritis, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic, phobias, obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception such as fibromyalgia; mood disorders such as depression, including major depression, single episode depression, recurrent depression, child abuse induced depression, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress-induced headache; cancer, human immunodeficiency virus (HIV) infections; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease; gastrointestinal diseases such as ulcers, irritable bowel syndrome, Crohn's disease, spastic colon, diarrhea, and post operative ileus and colonic hypersensitivity associated by psychopathological disturbances or stress; eating disorders such as anorexia and bulimia nervosa; hemorrhagic stress; stress-induced psychotic episodes;

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- euthyroid sick syndrome; syndrome of inappropriate antidiarrhetic hormone (ADH); obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage (e.g., cerebral ischemia such as cerebral 5 hippocampal ischemia); excitotoxic neuronal damage; epilepsy; cardiovascular and heart related disorders including hypertension, tachycardia and congestive heart failure; stroke; immune dysfunctions including stress induced immune dysfunctions (e.g., stress 10 induced fevers, porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, and dysfunctions induced by confinement in chickens, sheering stress in sheep or human-animal interaction related stress in dogs); muscular spasms; urinary 15 incontinence; senile dementia of the Alzheimer's type; multiinfarct dementia; amyotrophic lateral sclerosis; chemical dependencies and addictions (e.g., dependencies on alcohol, cocaine, heroin, benzodiazepines, or other drugs); drug and alcohol 20 withdrawal symptoms; osteoporosis; psychosocial dwarfism and hypoglycemia in a mammal.

The present invention provides novel compounds which bind to corticotropin releasing factor 25 receptors, thereby altering the anxiogenic effects of CRF secretion. The compounds of the present invention are useful for the treatment of psychiatric disorders and neurological diseases, anxiety-related disorders, post-traumatic stress disorder, supranuclear palsy and 30 feeding disorders as well as treatment of immunological, cardiovascular or heart-related diseases and colonic hypersensitivity associated with psychopathological disturbance and stress in a mammal.

35 According to another aspect, the present invention provides novel compounds of Formulae (1) and

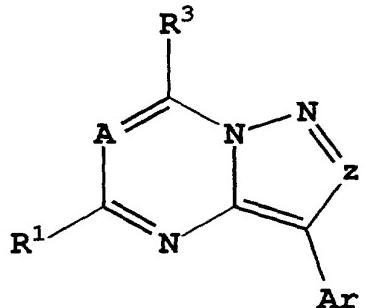
(2) (described below) which are useful as antagonists of the corticotropin releasing factor. The compounds of the present invention exhibit activity as corticotropin releasing factor antagonists and appear
5 to suppress CRF hypersecretion. The present invention also includes pharmaceutical compositions containing such compounds of Formulae (1) and (2), and methods of using such compounds for the suppression of CRF hypersecretion, and/or for the treatment of anxiogenic
10 disorders.

According to yet another aspect of the invention, the compounds provided by this invention (and especially labelled compounds of this invention)
15 are also useful as standards and reagents in determining the ability of a potential pharmaceutical to bind to the CRF receptor.

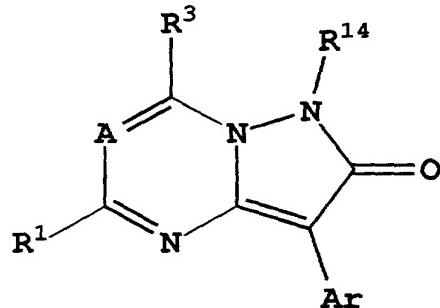
20 DETAILED DESCRIPTION OF INVENTION

[1] The present invention comprises a method of treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency
25 virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF,
30 including but not limited to disorders induced or facilitated by CRF, in mammals comprising
35

administering to the mammal a therapeutically effective amount of a compound of Formulae (1) or (2):



(1)



(2)

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and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof, wherein:

10

A is N or CR;

Z is N or CR²;

15

Ar is selected from phenyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, furanyl, thienyl, benzothienyl, benzofuranyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-benzopyranyl, tetralinyl, each Ar optionally substituted with 1 to 5 R⁴ groups and each Ar is attached to an unsaturated carbon atom;

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R is independently selected at each occurrence from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₇ cycloalkylalkyl, halo, CN, C₁-C₄ haloalkyl;

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- R¹ is independently selected at each occurrence from
 H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl,
 halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl,
 5 C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆
 cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-
 C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;
- R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-
 10 C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀
 cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -
 NR⁶R⁷, NR⁹COR¹⁰, -NR⁶S(O)_nR⁷, S(O)_nNR⁶R⁷, C₁-
 C₄ haloalkyl, -OR⁷, SH or -S(O)_nR¹²;
- 15 R³ is selected from:
 -H, OR⁷, SH, S(O)_nR¹³, COR⁷, CO₂R⁷,
 OC(O)R¹³, NR⁸COR⁷, N(COR⁷)₂, NR⁸CONR⁶R⁷,
 NR⁸CO₂R¹³, NR⁶R⁷, NR^{6a}R^{7a}, N(OR⁷)R⁶,
 CONR⁶R⁷, aryl, heteroaryl and heterocyclyl,
 20 or
 -C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl,
 C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₄-
 C₁₂ cycloalkylalkyl or C₆-C₁₀
 cycloalkenylalkyl, each optionally
 25 substituted with 1 to 3 substituents
 independently selected at each occurrence
 from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo,
 C₁-C₄ haloalkyl, cyano, OR¹⁵, SH,
 S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³,
 30 NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
 heteroaryl and heterocyclyl;
- R⁴ is independently selected at each occurrence from:
 35 C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl,
 C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, NO₂,

[REDACTED]

halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, NR⁸COR⁷,
 NR⁸CO₂R⁷, COR⁷, OR⁷, CONR⁶R⁷, CO(NOR⁹)R⁷, CO₂R⁷,
 or S(O)_nR⁷, where each such C₁-C₁₀ alkyl, C₂-
 C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl
 5 and C₄-C₁₂ cycloalkylalkyl are optionally
 substituted with 1 to 3 substituents
 independently selected at each occurrence from
 C₁-C₄ alkyl, NO₂, halo, CN, NR⁶R⁷, NR⁸COR⁷,
 NR⁸CO₂R⁷, COR⁷ OR⁷, CONR⁶R⁷, CO₂R⁷, CO(NOR⁹)R⁷,
 10 or S(O)_nR⁷;

R⁶ and R⁷, R^{6a} and R^{7a} are independently selected at
 each occurrence from:

[REDACTED]

-H,
 15 -C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
 C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
 alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
 C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
 or C₆-C₁₄ cycloalkenylalkyl, each
 20 optionally substituted with 1 to 3
 substituents independently selected at each
 occurrence from C₁-C₆ alkyl, C₃-
 C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
 cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
 25 OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
 heteroaryl or heterocyclyl,
 -aryl, aryl(C₁-C₄ alkyl), heteroaryl,
 heteroaryl(C₁-C₄ alkyl), heterocyclyl or
 30 heterocyclyl(C₁-C₄ alkyl);

alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently
 piperidine, pyrrolidine, piperazine, N-
 methylpiperazine, morpholine or thiomorpholine, each
 35 optionally substituted with 1-3 C₁-C₄ alkyl groups;

- R⁸ is independently selected at each occurrence from H or C₁-C₄ alkyl;
- 5 R⁹ and R¹⁰ are independently selected at each occurrence from H, C₁-C₄ alkyl, or C₃-C₆ cycloalkyl;
- 10 R¹¹ is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl, or C₃-C₆ cycloalkyl;
- R¹² is C₁-C₄ alkyl or C₁-C₄ haloalkyl;
- 15 R¹³ is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-, heteroaryl or heteroaryl(C₁-C₄ alkyl)-;
- 20 R¹⁴ is selected from C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₃-C₈ cycloalkyl, or C₄-C₁₂ cycloalkylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, and C₁-C₆ alkylthio, C₁-C₆ alkylsulfinyl and C₁-C₆ alkylsulfonyl;
- 25 R¹⁵ and R¹⁶ are independently selected at each occurrence from H, C₁-C₆ alkyl, C₃-C₁₀ cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that for S(O)_nR¹⁵, R¹⁵ cannot be H;

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- aryl is phenyl or naphthyl, each optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;
- 10 heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-dihydrobenzothienyl or 2,3-dihydrobenzofuranyl, each being optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, -COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;
- 25 heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and CONR¹⁶R¹⁵;
- 30 n is independently at each occurrence 0, 1 or 2,
- 35 [2] Preferred methods of the present invention are methods in wherein in the compound of Formulae (1) or

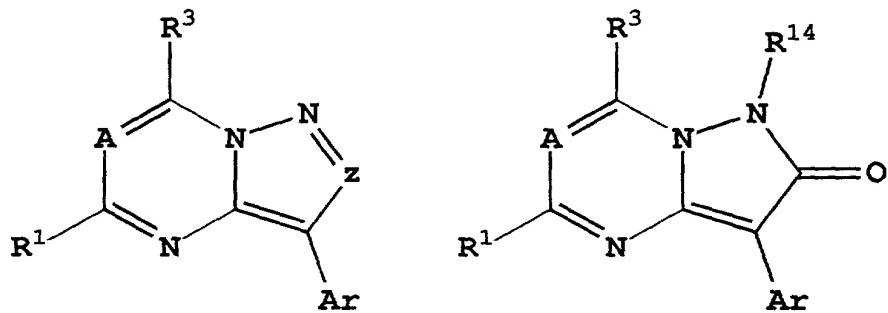
(2), Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, each optionally substituted with 1 to 4 R⁴ substituents.

- 5 [3] Further preferred methods of the above invention
are methods wherein, in the compound of Formulae (1)
or (2), A is N, Z is CR², Ar is 2,4-dichlorophenyl,
2,4-dimethylphenyl or 2,4,6-trimethylphenyl, R¹ and R²
are CH₃, and R³ is NR^{6a}R^{7a}.

10

[4] The present invention comprises compounds of Formulae (1) or (2):

15



(1)

(2)

and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and
20 pharmaceutically acceptable salt or pro-drug forms thereof wherein:

A is N or CR;

25 z is N or CR²;

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- Ar is selected from phenyl, naphthyl, pyridyl,
 pyrimidinyl, triazinyl, furanyl, thienyl,
 benzothienyl, benzofuranyl, 2,3-
 dihydrobenzofuranyl, 2,3-dihydrobenzothienyl,
 5 indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-
 benzopyranyl, tetrailinyl, each Ar optionally
 substituted with 1 to 5 R⁴ groups and each Ar is
 attached to an unsaturated carbon atom;
- 10 R is independently selected at each occurrence from H,
 C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆
 cycloalkyl, C₄-C₇ cycloalkylalkyl, halo, CN, C₁-
 C₄ haloalkyl;
- 15 R¹ is independently selected at each occurrence from
 H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl,
 halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl,
 C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆
 cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-
 20 C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;
- R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-
 C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀
 cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -
 25 NR⁶R⁷, NR⁹COR¹⁰, -NR⁶S(O)_nR⁷, S(O)_nNR⁶R⁷, C₁-
 C₄ haloalkyl, -OR⁷, SH or -S(O)_nR¹²;
- R³ is selected from:
 -H, OR⁷, SH, S(O)_nR¹³, COR⁷, CO₂R⁷,
 30 OC(O)R¹³, NR⁸COR⁷, N(COR⁷)₂, NR⁸CONR⁶R⁷,
 NR⁸CO₂R¹³, NR⁶R⁷, NR⁶aR⁷a, N(OR⁷)R⁶,
 CONR⁶R⁷, aryl, heteroaryl and
 heterocyclyl, or
 -C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl,
 35 C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₄-
 C₁₂ cycloalkylalkyl or C₆-C₁₀

10 R⁴ is independently selected at each occurrence from:
C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl,
C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, NO₂,
halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, NR⁸COR⁷,
NR⁸CO₂R⁷, COR⁷, OR⁷, CONR⁶R⁷, CO(NOR⁹)R⁷, CO₂R⁷,
or S(O)_nR⁷, where each such C₁-C₁₀ alkyl, C₂-
C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl
and C₄-C₁₂ cycloalkylalkyl are optionally
substituted with 1 to 3 substituents
15
independently selected at each occurrence from
C₁-C₄ alkyl, NO₂, halo, CN, NR⁶R⁷, NR⁸COR⁷,
NR⁸CO₂R⁷, COR⁷ OR⁷, CONR⁶R⁷, CO₂R⁷, CO(NOR⁹)R⁷,
or S(O)_nR⁷;
20

25 R⁶ and R⁷, R^{6a} and R^{7a} are independently selected at each occurrence from:
-H,
-C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
30 alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
or C₆-C₁₄ cycloalkenylalkyl, each
optionally substituted with 1 to 3
substituents independently selected at each
35 occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,

cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,

- 5 -aryl, aryl(C₁-C₄ alkyl), heteroaryl,
 heteroaryl(C₁-C₄ alkyl), heterocyclyl or
 heterocyclyl(C₁-C₄ alkyl),
 alternatively, NR⁶R⁷ and NR⁶aR⁷a are independently
 piperidine, pyrrolidine, piperazine, N-
 10 methylpiperazine, morpholine or thiomorpholine, each
 optionally substituted with 1-3 C₁-C₄ alkyl groups;

R^8 is independently selected at each occurrence from H or C₁-C₄ alkyl;

- 15 R⁹ and R¹⁰ are independently selected at each occurrence from H, C₁-C₄ alkyl, or C₃-C₆ cycloalkyl;

20 R¹¹ is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl, or C₃-C₆ cycloalkyl;

R^{12} is C₁-C₄ alkyl or C₁-C₄ haloalkyl;

- 25 R¹³ is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-, heteroaryl or heteroaryl(C₁-C₄ alkyl)-;

30 R¹⁴ is selected from C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₃-C₈ cycloalkyl, or C₄-C₁₂ cycloalkylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano,

OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, and C₁-C₆ alkylthio, C₁-C₆ alkylsulfinyl and C₁-C₆ alkylsulfonyl;

5

R¹⁵ and R¹⁶ are independently selected at each occurrence from H, C₁-C₆ alkyl, C₃-C₁₀ cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that for S(O)_nR¹⁵, R¹⁵ cannot be H;

10

aryl is phenyl or naphthyl, each optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-

15

C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

20

heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-

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dihydrobenzothienyl or 2,3-dihydrobenzofuranyl, each being optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, -COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

30

heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5

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- substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and CONR¹⁶R¹⁵;
- n is independently at each occurrence 0, 1 or 2,
- 10 with the provisos that:
- (1) when A is N, Z is CR², R² is H, R³ is -OR⁷ or -OCOR¹³, and R⁷ is H, then R¹ is not H, OH or SH;
 - (2) when A is N, Z is CR², R¹ is CH₃ or C₂H₅, R² is H, and R³ is OH, H, CH₃, C₂H₅, C₆H₅, n-C₃H₇, i-C₃H₇, SH, SCH₃, NHC₄H₉, or N(C₂H₅)₂, then Ar is not phenyl or m-CH₃-phenyl;
 - (3) when A is N, Z is CR², R² is H, and Ar is pyridyl, pyrimidinyl or pyrazinyl, and R³ is NR^{6a}R^{7a}, then R^{6a} and R^{7a} are not H or alkyl;
 - (4) when A is N, Z is CR², and R² is SO₂NR⁶R⁷, then R³ is not OH or SH;
 - (5) when A is CR and Z is CR², then R² is not-NR⁶SO₂R⁷ or -SO₂NR⁶R⁷;
 - (6) when A is N, Z is CR² and R² is -NR⁶SO₂R⁷ or -SO₂NR⁶R⁷, then R³ is not OH or SH;
 - (7) when A is N, Z is CR², R¹ is methyl or ethyl, R² is H, and R³ is H, OH, CH₃, C₂H₅, C₆H₅, n-C₃H₇, iso-C₃H₇, SH, SCH₃, NH(n-C₄H₉), or N(C₂H₅)₂, then Ar is not unsubstituted phenyl or m-methylphenyl;

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- (8) when A is CR, Z is CR², R² is H, phenyl or alkyl, R³ is NR⁸COR⁷ and Ar is phenyl or phenyl substituted with phenylthio, then R⁷ is not aryl, aryl(C₁-C₄ alkyl), heteroaryl, heteroaryl(C₁-C₄ alkyl), heterocyclyl or heterocyclyl(C₁-C₄ alkyl);
 - 5
 - (9) when A is CR, Z is CR², R² is H or alkyl, Ar is phenyl, and R³ is SR¹³ or NR^{6a}R^{7a}, then R¹³ is not aryl or heteroaryl and R^{6a} and R^{7a} are not H or 10 aryl; or
 - (10) when A is CH, Z is CR², R¹ is OR¹¹, R² is H, R³ is OR⁷, and R⁷ and R¹¹ are both H, then Ar is not phenyl, p-Br-phenyl, p-Cl-phenyl, p-NHCOCH₃-phenyl, p-CH₃-phenyl, pyridyl or naphthyl;
 - 15
 - (11) when A is CH, Z is CR², R² is H, Ar is unsubstituted phenyl, and R³ is CH₃, C₂H₅, CF₃ or C₆H₄F, then R₁ is not CF₃ or C₂F₅;
 - 20
 - (12) when A is CR, R is H, Z is CR², R² is OH, and R¹ and R³ are H, then Ar is not phenyl;
 - (13) when A is CR, R is H, Z is CR², R² is OH or NH₂, R¹ and R³ are CH₃, then Ar is not 4-phenyl-3-cyano-2-aminopyrid-2-yl.
 - 25

[5] Preferred compounds of the above invention are compounds of Formulae (1) and (2) and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof with the additional provisos that: (1) when A is N, R¹ is H, C₁-C₄ alkyl, halo, CN, C₁-C₁₂ hydroxyalkyl, C₁-C₄ alkoxyalkyl or SO₂(C₁-C₄ alkyl), R³ is NR^{6a}R^{7a} and R^{6a} is unsubstituted C₁-C₄ alkyl, then R^{7a} is not phenyl,

naphthyl, thienyl, benzothienyl, pyridyl, quinolyl,
pyrazinyl, furanyl, benzofuranyl, benzothiazolyl,
indolyl or C₃-C₆ cycloalkyl; and (2) A is N, R¹ is H,
C₁-C₄ alkyl, halo, CN, C₁-C₁₂ hydroxyalkyl, C₁-C₄

- 5 alkoxyalkyl or SO₂(C₁-C₄ alkyl), R³ is NR^{6a}R^{7a} and R^{7a}
is unsubstituted C₁-C₄ alkyl, then R^{6a} is not phenyl,
naphthyl, thienyl, benzothienyl, pyridyl, quinolyl,
pyrazinyl, furanyl, benzofuranyl, benzothiazolyl,
indolyl or C₃-C₆ cycloalkyl.

10

- [6] Preferred compounds of the above invention also
include compounds of Formulae (1) and (2) and isomers
thereof, stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
15 acceptable salt or pro-drug forms thereof wherein Ar
is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, each
optionally substituted with 1 to 4 R⁴ substituents.

- [7]. Preferred compounds of the above invention also
20 include compounds of Formulae (1) and (2) and isomers
thereof, stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein A is
N, Z is CR², Ar is 2,4-dichlorophenyl, 2,4-
25 dimethylphenyl or 2,4,6-trimethylphenyl, R¹ and R² are
CH₃, and R³ is NR^{6a}R^{7a}.

- [11] More preferred compounds of the above invention are
compounds and isomers thereof, stereoisomeric forms
30 thereof, or mixtures of stereoisomeric forms thereof,
and pharmaceutically acceptable salt or pro-drug forms
thereof wherein A is N.

- [12] More preferred compounds of the above invention
35 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of

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stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof.

[13] More preferred compounds of the above invention
5 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein Ar is
phenyl, pyridyl or 2,3-dihydrobenzofuranyl and each Ar
10 is optionally substituted with 1 to 4 R⁴ substituents.

[14] More preferred compounds of the above invention
also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein R³ is
NR^{6a}R^{7a} or OR⁷.

[15] More preferred compounds of the above invention
20 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein Ar is
phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar
25 is optionally substituted with 1 to 4 R⁴ substituents,
and R³ is NR^{6a}R^{7a} or OR⁷.

[16] More preferred compounds of the above invention
also include compounds and isomers thereof,
30 stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein Z is
CR².

35 [17] More preferred compounds of the above invention
also include compounds and isomers thereof,

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stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl and each Ar 5 is optionally substituted with 1 to 4 R⁴ substituents.

[18] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of 10 stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R³ is NR^{6a}R^{7a} or OR⁷.

[19] More preferred compounds of the above invention 15 also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R^{6a} is independently selected from:

20 -H,
 -C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
 C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
 alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
 C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
 or C₆-C₁₄ cycloalkenylalkyl, each
 optionally substituted with 1 to 3
 substituents independently selected at each
 occurrence from C₁-C₆ alkyl, C₃-
 C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
 30 cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
 OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
 heteroaryl or heterocyclyl,
 -aryl, aryl(C₁-C₄ alkyl)-, heteroaryl, heteroaryl(C₁-
 35 C₄ alkyl)-, heterocyclyl or heterocyclyl(C₁-C₄
 alkyl)-; and

CO_2R^{15} , OC(O)R^{13} , $\text{NR}^8\text{COR}^{15}$, $\text{N}(\text{COR}^{15})_2$,
 $\text{NR}^8\text{CONR}^{16}\text{R}^{15}$, $\text{NR}^8\text{CO}_2\text{R}^{13}$, $\text{NR}^{16}\text{R}^{15}$, $\text{CONR}^{16}\text{R}^{15}$,
 aryl, heteroaryl or heterocyclyl, and
 -aryl or heteroaryl.

5

[21] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R^{6a} is selected from:

-H,
 -C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
 C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
 15 alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
 C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
 or C₆-C₁₄ cycloalkenylalkyl, each
 optionally substituted with 1 to 3
 substituents independently selected at each
 20 occurrence from C₁-C₆ alkyl, C₃-
 C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
 cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
 OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
 25 heteroaryl or heterocyclyl,
 -aryl, aryl(C₁-C₄ alkyl), heteroaryl,
 heteroaryl(C₁-C₄ alkyl), heterocyclyl or
 heterocyclyl(C₁-C₄ alkyl);

25

R^{7a} is selected from:

30 -C₁-C₄ alkyl and each such C₁-C₄ alkyl is
 substituted with 1-3 substituents
 independently selected at each occurrence from
 C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
 haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
 35 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,

NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl.

- [22] More preferred compounds of the above invention
5 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein
one of R^{6a} and R^{7a} is selected from:
10 -C₃-C₆ cycloalkyl, each such C₃-C₆ cycloalkyl
optionally substituted with 1-3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
15 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl,
-aryl,
-heteroaryl or
20 -heterocyclyl,
and the other of R^{6a} and R^{7a} is unsubstituted C₁-C₄
alkyl.

- [23] More preferred compounds of the above invention
25 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein
R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl,
30 each such C₁-C₁₀ alkyl optionally substituted with
1 to 3 substituents independently selected at each
occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³,
COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,

R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.

[24] More preferred compounds of the above invention
 5 also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar
 10 is optionally substituted with 1 to 4 R⁴ substituents, and R³ is NR^{6a}R^{7a} or OR⁷.

[25] More preferred compounds of the above invention also include compounds and isomers thereof,
 15 stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R^{6a} is independently selected from:
 -H,
 20 -C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each
 25 optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 30 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl, -aryl, aryl(C₁-C₄ alkyl)-, heteroaryl, heteroaryl(C₁-C₄ alkyl), heterocyclyl or
 35 heterocyclyl(C₁-C₄ alkyl);

- R^{7a} is independently selected at each occurrence from:
- H,
 - C₅-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
 - 5 C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl,
 - 10 -aryl, aryl(C₁-C₄ alkyl), heteroaryl, heteroaryl(C₁-C₄ alkyl), heterocyclyl or heterocyclyl(C₁-C₄ alkyl),
 - 15 alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each optionally substituted with 1-3 C₁-C₄ alkyl groups.
 - 20 [26] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R^{6a} and R^{7a} are identical and are selected from:
 - 25 -C₁-C₄ alkyl or C₃-C₆ cycloalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, -COR¹⁵,
 - 30
 - 35

CO_2R^{15} , OC(O)R^{13} , $\text{NR}^8\text{COR}^{15}$, $\text{N}(\text{COR}^{15})_2$,
 $\text{NR}^8\text{CONR}^{16}\text{R}^{15}$, $\text{NR}^8\text{CO}_2\text{R}^{13}$, $\text{NR}^{16}\text{R}^{15}$, $\text{CONR}^{16}\text{R}^{15}$,
aryl, heteroaryl or heterocyclyl, and
-aryl or heteroaryl.

5

[27] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R^{6a} and R^{7a} are identical and are

-C₁-C₄ alkyl, each such C₁-C₄ alkyl

optionally substituted with 1 to 3

substituents independently selected at each

occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, -COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.

15

[28] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R^{6a} is selected from:

-H,

-C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,

C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈

30

alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-

C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,

or C₆-C₁₄ cycloalkenylalkyl, each

optionally substituted with 1 to 3

substituents independently selected at each

35

occurrence from C₁-C₆ alkyl, C₃-

C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,

5 heteroaryl or heterocyclyl,
-aryl, aryl(C₁-C₄ alkyl), heteroaryl,
heteroaryl(C₁-C₄ alkyl), heterocyclyl or
heterocyclyl(C₁-C₄ alkyl);

R^{7a} is:
10 -C₁-C₄ alkyl and each such C₁-C₄ alkyl is
substituted with 1-3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
15 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl.

[29] More preferred compounds of the above invention
20 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein one of
R^{6a} and R^{7a} is selected from:
25 -C₃-C₆ cycloalkyl, each such C₃-C₆ cycloalkyl
optionally substituted with 1-3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
30 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl,
-aryl,
-heteroaryl or
35 -heterocyclyl,

and the other of R^{6a} and R^{7a} is unsubstituted C₁-C₄ alkyl.

[30] More preferred compounds of the above invention
5 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein
R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl,
10 each such C₁-C₁₀ alkyl optionally substituted with
1 to 3 substituents independently selected at each
occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³,
COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
15 R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
heteroaryl or heterocyclyl.

[31] More preferred compounds of the above invention
also include compounds and isomers thereof,
20 stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein
-Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
25 to 4 R⁴ substituents,
-R³ is NR^{6a}R^{7a} or OR⁷ and
-R¹ and R² are independently selected from H, C₁-C₄
alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀
cycloalkylalkyl.

30 [32] More preferred compounds of the above invention
also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
35 acceptable salt or pro-drug forms thereof wherein

R^{6a} is independently selected from:

- H,
- C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
- C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
- 5 alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
- C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
- or C₆-C₁₄ cycloalkenylalkyl, each
- optionally substituted with 1 to 3
- substituents independently selected at each
- 10 occurrence from C₁-C₆ alkyl, C₃-
- C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
- cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
- OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
- NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
- 15 heteroaryl or heterocyclyl,
- aryl, aryl(C₁-C₄ alkyl)-, heteroaryl, heteroaryl(C₁-
- C₄ alkyl), heterocyclyl or heterocyclyl(C₁-C₄
- alkyl);

R^{7a} is independently selected at each occurrence from:

- 20 -H,
- C₅-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
- C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
- alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
- C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
- 25 or C₆-C₁₄ cycloalkenylalkyl, each
- optionally substituted with 1 to 3
- substituents independently selected at each
- occurrence from C₁-C₆ alkyl, C₃-
- C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
- cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
- 30 OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
- NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
- heteroaryl or heterocyclyl,

-aryl, aryl(C₁-C₄ alkyl), heteroaryl,
heteroaryl(C₁-C₄ alkyl), heterocyclyl or
heterocyclyl(C₁-C₄ alkyl),

- 5 alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently
piperidine, pyrrolidine, piperazine, N-
methylpiperazine, morpholine or thiomorpholine, each
optionally substituted with 1-3 C₁-C₄ alkyl groups.
- 10 [33] More preferred compounds of the above invention
also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein R^{6a}
15 and R^{7a} are identical and are selected from:
-C₁-C₄ alkyl or C₃-C₆ cycloalkyl, each optionally
substituted with 1 to 3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
20 haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, -COR¹⁵,
CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl, and
-aryl or heteroaryl.
- 25 [34] More preferred compounds of the above invention
also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein R^{6a}
30 and R^{7a} are identical and are
-C₁-C₄ alkyl, each such C₁-C₄ alkyl
optionally substituted with 1 to 3
substituents independently selected at each
35 occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,

halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH,
 S(O)_nR¹³, -COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵,
 N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵,
 CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.

5

[35] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R^{6a} is selected from:

-H,
 -C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
 C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
 15 alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
 C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
 or C₆-C₁₄ cycloalkenylalkyl, each
 optionally substituted with 1 to 3
 substituents independently selected at each
 20 occurrence from C₁-C₆ alkyl, C₃-
 C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
 cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
 OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
 NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
 25 heteroaryl or heterocyclyl,
 -aryl, aryl(C₁-C₄ alkyl), heteroaryl,
 heteroaryl(C₁-C₄ alkyl), heterocyclyl or
 heterocyclyl(C₁-C₄ alkyl);

R^{7a} is:

30 -C₁-C₄ alkyl and each such C₁-C₄ alkyl is
 substituted with 1-3 substituents
 independently selected at each occurrence from
 C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
 haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
 35 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,

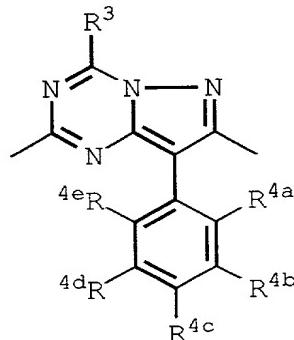
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl.

- [36] More preferred compounds of the above invention
5 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein one of
R^{6a} and R^{7a} is selected from:
10 -C₃-C₆ cycloalkyl, each such C₃-C₆ cycloalkyl
optionally substituted with 1-3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
15 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl,
-aryl,
-heteroaryl or
20 -heterocyclyl,
and the other of R^{6a} and R^{7a} is unsubstituted C₁-C₄
alkyl.

- [37] More preferred compounds of the above invention
25 also include compounds and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt or pro-drug forms thereof wherein
R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl,
30 each such C₁-C₁₀ alkyl optionally substituted with
1 to 3 substituents independently selected at each
occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³,
COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,

$R^8CONR^{16}R^{15}$, $NR^8CO_2R^{13}$, $NR^{16}R^{15}$, $CONR^{16}R^{15}$, aryl, heteroaryl or heterocyclyl.

[38] Specifically preferred compounds of the above
5 invention are compounds of Formula (50)



FORMULA (50)

10

and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms
15 thereof, selected from the group consisting of:

a compound of Formula (50) wherein R^3 is $-NHCH(n-Pr)_2$,
20 R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R^3 is $-N(Et)(n-Bu)$,
25 R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (50) wherein R^3 is $-(n-Pr)(CH_2cPr)$, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R^3 is $-N(CH_2CH_2OMe)_2$,
35 R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is -NHCH(Et)(n-Bu), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -NHCH(CH₂OEt)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -N(Me)(Ph), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -N(n-Pr)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(Et)(n-Pr), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -OEt, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NHCH(Me)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -OCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -NHCH(Me)(CH₂N(Me)₂), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is Me, R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -N(cPr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -N(n-Bu)(CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 25 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R³ is -NHCH(CH₂CH₂OMe)(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 40 a compound of Formula (50) wherein R³ is morpholino, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 10 a compound of Formula (50) wherein R³ is -NH(c-Pr), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is CN, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 15 a compound of Formula (50) wherein R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 20 20 a compound of Formula (50) wherein R³ is -NCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;
- 25 25 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;
- 30 30 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 35 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 40 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

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- a compound of Formula (50) wherein a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -(c-Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -(S)-NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;
- 45 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NH(CH₂OMe)(CH₂-iPr), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is H, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is NMe₂, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)(n-Pr), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NHCH(CH₂OEt)(Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is NMe₂, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

- 5 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

10 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is NMe₂, R^{4d} is H and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is (S)-NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is (S)-NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is -N(Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is -NH(Et)(CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

45 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

50 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)(CH₂CH₂OH), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -N(CH₂C-Pr) (n-Pr), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -N(c-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -NHCH (Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is CN, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(CH₂OH)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H; and

a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H.

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[39] More specifically preferred is 4-(bis-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine and isomers thereof, stereoisomeric forms thereof, or
10 mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof.

[40] More specifically preferred is 4-(bis-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms
20 thereof.

[41] More preferred are compounds of the above invention are compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof,
25 and pharmaceutically acceptable salt or pro-drug forms thereof wherein A is CR.

[42] More preferred compounds of the above invention also include compounds and isomers thereof,
30 stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof.

[43] More preferred compounds of the above invention
35 also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of

stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl and each Ar is optionally substituted with 1 to 4 R⁴ substituents.

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- [44] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R³ is NR^{6a}R^{7a} or OR⁷.

- [45] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents, and R³ is NR^{6a}R^{7a} or OR⁷.

- [46] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein Z is CR².

- [47] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl and each Ar is optionally substituted with 1 to 4 R⁴ substituents.

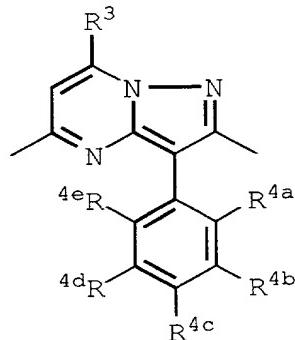
- [48] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R³ is NR^{6a}R^{7a} or OR⁷.
- 5
- [49] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents, and R³ is NR^{6a}R^{7a} or OR⁷.
- 10
- [50] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl, and each such C₁-C₁₀ alkyl is optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.
- 15
- 20
- 25
- 30
- [51] More preferred compounds of the above invention also include compounds and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof wherein
- 35

-Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
 and each Ar is optionally substituted with 1
 to 4 R⁴ substituents,
 -R³ is NR^{6a}R^{7a} or OR⁷ and
 5 -R¹ and R² are independently selected from H, C₁-C₄
 alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀
 cycloalkylalkyl.

[52] More preferred compounds of the above invention
 10 also include compounds and isomers thereof,
 stereoisomeric forms thereof, or mixtures of
 stereoisomeric forms thereof, and pharmaceutically
 acceptable salt or pro-drug forms thereof wherein
 R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl,
 15 and each such C₁-C₁₀ alkyl is optionally
 substituted with 1 to 3 substituents independently
 selected at each occurrence from C₁-C₆ alkyl, C₃-
 C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵,
 SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵,
 20 N(COR¹⁵)₂, R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵,
 CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.

[53] Specifically preferred compounds of the above
 invention are compounds of Formula (51)

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FORMULA (51)

- and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms
- 5 thereof selected from the group consisting of:
- a compound of Formula (51) wherein R³ is -NHCH(n-Pr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (51) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (51) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (51) wherein R³ is -N(C-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (51) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (51) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (51) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (51) wherein R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

- a compound of Formula (51) wherein R³ is -N(n-Bu) (CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (51) wherein R³ is -NHCH(n-Pr) (CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (51) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (51) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (51) wherein R³ is -(S)-NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (51) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (51) wherein R³ is -NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (51) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (51) wherein R³ is (S)-NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

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- a compound of Formula (51) wherein R³ is -
 NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Me, R^{4b} is H, R^{4c} is
 Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (51) wherein R³ is -N(n-
 Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d}
 is H and R^{4e} is H;
- 10 a compound of Formula (51) wherein R³ is -N(Et)₂, R^{4a} is
 Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (51) wherein R³ is (S) -
 NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is
 Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (51) wherein R³ is -NH(CH₂CH₂OMe)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is
 Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (51) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d}
 is H and R^{4e} is H;
- 30 a compound of Formula (51) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d}
 is H and R^{4e} is H;
- 35 a compound of Formula (51) wherein R³ is -NHCH(n-
 Pr)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d}
 is H and R^{4e} is H;
- 40 a compound of Formula (51) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
 H;

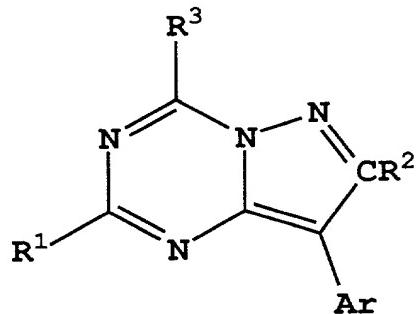
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- a compound of Formula (51) wherein R³ is -NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (51) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (51) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (51) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 20 a compound of Formula (51) wherein R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (51) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 25 a compound of Formula (51) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 30 a compound of Formula (51) wherein R³ is -N(Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 35 a compound of Formula (51) wherein R³ is -NHCH(Et)CH₂OMe, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (51) wherein R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

- a compound of Formula (51) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (51) wherein R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (51) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (51) wherein R³ is -NET₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
and
- 15 a compound of Formula (51) wherein R³ is -N(Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H.
- [54] More specifically preferred is 7-(3-
- 20 pentylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolopyrimidine and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof.
- 25 [55] More specifically preferred is 7-(Diethylamino)-2,5-dimethyl-3-(2-methyl-4-methoxyphenyl-[1,5-a]-pyrazolopyrimidine and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-
- 30 drug forms thereof.
- [56] More specifically preferred is 7-(N-(3-cyanopropyl)-N-propylamino)-2,5-dimethyl-3-(2,4-dimethylphenyl)-[1,5-a]-pyrazolopyrimidine and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt or pro-drug forms thereof.

The present invention also provides pharmaceutical compositions comprising compounds of Formulae (1) and (2) and a pharmaceutically acceptable carrier.

[1] The present invention still further comprises a method of treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in mammals comprising administering to the mammal a therapeutically effective amount of a compound of Formula (1):

25



and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof, wherein:

5

Ar is selected from phenyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, furanyl, thieryl, benzothienyl, benzofuranyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 10 indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-benzopyranyl, tetrainyl, each Ar optionally substituted with 1 to 5 R⁴ groups and each Ar is attached to an unsaturated carbon atom;

15 R¹ is independently selected at each occurrence from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl, C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-20 C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;

25 R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -NR⁶R⁷, NR⁹COR¹⁰, -NR⁶S(O)_nR⁷, S(O)_nNR⁶R⁷, C₁-C₄ haloalkyl, -OR⁷, SH or -S(O)_nR¹²;

R³ is selected from NR^{6a}R^{7a} and OR⁷;

30 R⁴ is independently selected at each occurrence from: C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, NO₂, halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, NR⁸COR⁷, NR⁸CO₂R⁷, COR⁷, OR⁷, CONR⁶R⁷, CO(NOR⁹)R⁷, CO₂R⁷, 35 or S(O)_nR⁷, where each such C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl

and C₄-C₁₂ cycloalkylalkyl are optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₄ alkyl, NO₂, halo, CN, NR⁶R⁷, NR⁸COR⁷, NR⁸CO₂R⁷, COR⁷ OR⁷, CONR⁶R⁷, CO₂R⁷, CO(NOR⁹)R⁷, or S(O)_nR⁷;

R⁶, R⁷, R^{6a} and R^{7a} are independently selected at each occurrence from:

- 10 -H,
- C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each
- 15 optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl, -aryl, aryl(C₁-C₄ alkyl), heteroaryl, heteroaryl(C₁-C₄ alkyl), heterocyclyl or heterocyclyl(C₁-C₄ alkyl);
- 20
- 25

alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each optionally substituted with 1-3 C₁-C₄ alkyl groups;

R⁸ is independently selected at each occurrence from H or C₁-C₄ alkyl;

35

- R⁹ and R¹⁰ are independently selected at each occurrence from H, C₁-C₄ alkyl, or C₃-C₆ cycloalkyl;
- 5 R¹¹ is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl, or C₃-C₆ cycloalkyl;
- R¹² is C₁-C₄ alkyl or C₁-C₄ haloalkyl;
- 10 R¹³ is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-, heteroaryl or heteroaryl(C₁-C₄ alkyl)-;
- 15 R¹⁵ and R¹⁶ are independently selected at each occurrence from H, C₁-C₆ alkyl, C₃-C₁₀ cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that for S(O)_nR¹⁵, R¹⁵ cannot be H;
- 20 aryl is phenyl or naphthyl, each optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;
- 25 heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-dihydrobenzothienyl or 2,3-dihydrobenzofuranyl, each being optionally substituted with 1 to 5

5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, -COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

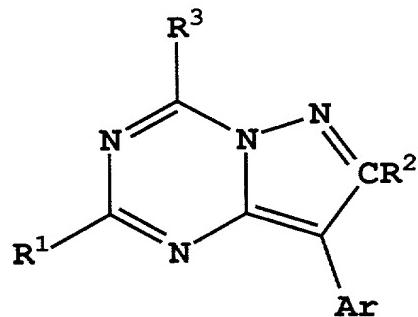
10 heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and
15 CONR¹⁶R¹⁵;

n is independently at each occurrence 0, 1 or 2.

20 [2] Further preferred methods of the present invention are methods of claim 1 wherein, in the compound of Formula (1), Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, each optionally substituted with 1 to 4 R⁴ substituents.

25 [2] Further preferred methods of the present invention are methods of claim 1 wherein, in the compound of Formula (1), Ar is 2,4-dichlorophenyl, 2,4-dimethylphenyl or 2,4,6-trimethylphenyl, R¹ and R² are CH₃, and R³ is NR^{6a}R^{7a}.

30 [4] The present invention further comprises compounds of Formula (1):



(1)

and isomers thereof, stereoisomeric forms thereof, or
 5 mixtures of stereoisomeric forms thereof, and
 pharmaceutically acceptable salt forms thereof
 wherein:

Ar is selected from phenyl, naphthyl, pyridyl,
 10 pyrimidinyl, triazinyl, furanyl, thienyl,
 benzothienyl, benzofuranyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl,
 indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-benzopyranyl, tetralinyl, each Ar optionally
 15 substituted with 1 to 5 R⁴ groups and each Ar is
 attached to an unsaturated carbon atom;

R¹ is independently selected at each occurrence from
 H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl,
 20 halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl,
 C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆
 cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;

25 R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -

NR^6R^7 , $\text{NR}^9\text{COR}^{10}$, $-\text{NR}^6\text{S(O)}_n\text{R}^7$, $\text{S(O)}_n\text{NR}^6\text{R}^7$, C_1-
 C_4 haloalkyl, $-\text{OR}^7$, SH or $-\text{S(O)}_n\text{R}^{12}$;

R^3 is selected from $\text{NR}^6\text{aR}^7\text{a}$ and OR^7 ;

5

R^4 is independently selected at each occurrence from:

C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl,
 C_3-C_6 cycloalkyl, C_4-C_{12} cycloalkylalkyl, NO_2 ,
halo, CN, C_1-C_4 haloalkyl, NR^6R^7 , NR^8COR^7 ,

10 $\text{NR}^8\text{CO}_2\text{R}^7$, COR^7 , OR^7 , CONR^6R^7 , $\text{CO(NOR}^9\text{)R}^7$, CO_2R^7 ,
or $\text{S(O)}_n\text{R}^7$, where each such C_1-C_{10} alkyl, C_2-
 C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_6 cycloalkyl
and C_4-C_{12} cycloalkylalkyl are optionally

substituted with 1 to 3 substituents

15

independently selected at each occurrence from
 C_1-C_4 alkyl, NO_2 , halo, CN, NR^6R^7 , NR^8COR^7 ,
 $\text{NR}^8\text{CO}_2\text{R}^7$, COR^7 OR^7 , CONR^6R^7 , CO_2R^7 , $\text{CO(NOR}^9\text{)R}^7$,
or $\text{S(O)}_n\text{R}^7$;

20 R^6 , R^7 , R^6a and R^7a are independently selected at each
occurrence from:

-H,

$-\text{C}_1-\text{C}_{10}$ alkyl, C_3-C_{10} alkenyl, C_3-C_{10} alkynyl,

C_1-C_{10} haloalkyl with 1-10 halogens, C_2-C_8

25

alkoxyalkyl, C_3-C_6 cycloalkyl, C_4-

C_{12} cycloalkylalkyl, C_5-C_{10} cycloalkenyl,

or C_6-C_{14} cycloalkenylalkyl, each

optionally substituted with 1 to 3

substituents independently selected at each
occurrence from C_1-C_6 alkyl, C_3-

30

C_6 cycloalkyl, halo, C_1-C_4 haloalkyl,

cyano, OR^{15} , SH, $\text{S(O)}_n\text{R}^{13}$, COR^{15} , CO_2R^{15} ,

$\text{OC(O)}\text{R}^{13}$, $\text{NR}^8\text{COR}^{15}$, $\text{N}(\text{COR}^{15})_2$, $\text{NR}^8\text{CONR}^{16}\text{R}^{15}$,

$\text{NR}^8\text{CO}_2\text{R}^{13}$, $\text{NR}^{16}\text{R}^{15}$, $\text{CONR}^{16}\text{R}^{15}$, aryl,

35

heteroaryl or heterocyclyl,

-aryl, aryl(C₁-C₄ alkyl), heteroaryl,
heteroaryl(C₁-C₄ alkyl), heterocyclyl or
heterocyclyl(C₁-C₄ alkyl),

alternatively, NR⁶R⁷ and NR⁶aR⁷a are independently
5 piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each
optionally substituted with 1-3 C₁-C₄ alkyl groups;

R⁸ is independently selected at each occurrence from H or C₁-C₄ alkyl;

R^9 and R^{10} are independently selected at each occurrence from H, C₁-C₄ alkyl, or C₃-C₆ cycloalkyl;

15 R¹¹ is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl,
or C₃-C₆ cycloalkyl;

R^{12} is C₁-C₄ alkyl or C₁-C₄ haloalkyl;

20 R¹³ is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-, heteroaryl or heteroaryl(C₁-C₄ alkyl)-;

25 R¹⁵ and R¹⁶ are independently selected at each occurrence from H, C₁-C₆ alkyl, C₃-C₁₀ cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that for S(O)_nR¹⁵, R¹⁵ cannot be H;

30 aryl is phenyl or naphthyl, each optionally substituted with 1 to 5 substituents

35 C6 cycloalkyl, halo, C1-C4 haloalkyl, cyano,

OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

5 heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-
10 dihydrobenzothienyl or 2,3-dihydrobenzofuranyl, each being optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, -COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

20 heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and CONR¹⁶R¹⁵;

25 n is independently at each occurrence 0, 1 or 2;

30 with the provisos that:

- (1) when R² is H and R³ is -OR⁷ and R⁷ is H, then R¹ is not H, OH or SH;

- (2) when R^1 is CH_3 or C_2H_5 and R^2 is H, and R^3 is OH, NHC_4H_9 , or $N(C_2H_5)_2$, then Ar is not phenyl or m- CH_3 -phenyl;
- 5 (3) when R^2 is H and Ar is pyridyl, pyrimidinyl or pyrazinyl, and R^3 is $NR^{6a}R^{7a}$, then R^{6a} and R^{7a} are not H or alkyl;
- 10 (4) when R^2 is $SO_2NR^6R^7$, then R^3 is not OH; and
- 10 (5) when R^2 is $-NR^6SO_2R^7$ or $-SO_2NR^6R^7$, then R^3 is not OH.

15 [5] Further preferred compounds of the present invention include compounds of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof with the additional provisos that: (1) when R^1 is H, C₁-C₄ alkyl, halo, CN, C₁-C₁₂ hydroxyalkyl, C₁-C₄ alkoxyalkyl or $SO_2(C_1-C_4$ alkyl) and R^3 is $NR^{6a}R^{7a}$ and R^{6a} is unsubstituted C₁-C₄ alkyl, then R^{7a} is not phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, indolyl or C₃-C₆ cycloalkyl; and (2) when R^1 is H, C₁-C₄ alkyl, halo, CN, C₁-C₁₂ hydroxyalkyl, C₁-C₄ alkoxyalkyl or $SO_2(C_1-C_4$ alkyl) and R^3 is $NR^{6a}R^{7a}$ and R^{7a} is unsubstituted C₁-C₄ alkyl, then R^{6a} is not phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, indolyl or C₃-C₆ cycloalkyl.

30 [6] Further preferred compounds of the present invention include compounds of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of

stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein: Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, each optionally substituted with 1 to 4 R⁴ substituents.

5

- [7] Further preferred compounds of the present invention include compounds of claim 6 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein: Ar is 2,4-dichlorophenyl, 2,4-dimethylphenyl or 2,4,6-trimethylphenyl, and R¹ and R² are CH₃.

- [8] The present invention further provides for a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 4.

- [9] The present invention further provides for a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 6.

- [10] The present invention further provides for a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 7.

- [11] Further preferred compounds of the present invention include compounds of claim 6 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

- 35 R^{6a} is independently selected from:
-H,

-C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
or C₆-C₁₄ cycloalkenylalkyl, each
optionally substituted with 1 to 3
substituents independently selected at each
occurrence from C₁-C₆ alkyl, C₃-
C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
heteroaryl or heterocyclyl,
-aryl, aryl(C₁-C₄ alkyl)-, heteroaryl,
heteroaryl(C₁-C₄ alkyl)-, heterocyclyl or
heterocyclyl(C₁-C₄ alkyl)-; and
R^{7a} is independently selected at each occurrence from:
-H,
-C₅-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈
alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
or C₆-C₁₄ cycloalkenylalkyl, each
optionally substituted with 1 to 3
substituents independently selected at each
occurrence from C₁-C₆ alkyl, C₃-
C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
heteroaryl or heterocyclyl,
-aryl, aryl(C₁-C₄ alkyl), heteroaryl,
heteroaryl(C₁-C₄ alkyl), heterocyclyl or
heterocyclyl(C₁-C₄ alkyl);

alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each optionally substituted with 1-3 C₁-C₄ alkyl groups.

5

- [12] Further preferred compounds of the present invention include compounds of claim 6 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

R^{6a} and R^{7a} are identical and are selected from:

-C₁-C₄ alkyl or C₃-C₆ cycloalkyl, each optionally substituted with 1 to 3 substituents

- 15 independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, -COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
- 20 aryl, heteroaryl or heterocyclyl, and -aryl or heteroaryl.

- [13] Further preferred compounds of the present invention include compounds of claim 6 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

R^{6a} is selected from:

- 30 -H,
-C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
35 or C₆-C₁₄ cycloalkenylalkyl, each

optionally substituted with 1 to 3
substituents independently selected at each
occurrence from C₁-C₆ alkyl, C₃-
C₆ cycloalkyl, halo, C₁-C₄ haloalkyl,
5 cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵,
OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,
NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
heteroaryl or heterocyclyl,
-aryl, aryl(C₁-C₄ alkyl), heteroaryl,
10 heteroaryl(C₁-C₄ alkyl), heterocyclyl or
heterocyclyl(C₁-C₄ alkyl);

R^{7a} is selected from:
-C₁-C₄ alkyl and each such C₁-C₄ alkyl is
substituted with 1-3 substituents
15 independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
20 aryl, heteroaryl or heterocyclyl.

[14] Further preferred compounds of the present
invention include compounds of claim 6 and isomers
thereof, stereoisomeric forms thereof, or mixtures of
25 stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof wherein:

one of R^{6a} and R^{7a} is selected from:
-C₃-C₆ cycloalkyl, each such C₃-C₆ cycloalkyl
30 optionally substituted with 1-3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
35 NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl,

-aryl,
-heteroaryl or
-heterocyclyl,

and the other of R^{6a} and R^{7a} is unsubstituted C₁-C₄

5 alkyl.

[15] Further preferred compounds of the present invention include compounds of claim 6 and isomers thereof, stereoisomeric forms thereof, or mixtures of 10 stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl, each such C₁-C₁₀ alkyl optionally substituted with 1 to 3 substituents independently selected at each 15 occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.

20 [16] Further preferred compounds of the present invention include compounds of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:
25 -Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents;
-R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

30 [17] Further preferred compounds of the present invention include compounds of claim 11 and isomers thereof, stereoisomeric forms thereof, or mixtures of

stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

-Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
5 to 4 R⁴ substituents;

-R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

10 [18] Further preferred compounds of the present invention include compounds of claim 12 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

15 -Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents;

-R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

20 [19] Further preferred compounds of the present invention include compounds of claim 13 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

-Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents;

30 -R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

35 [20] Further preferred compounds of the present invention include compounds of claim 14 and isomers thereof, stereoisomeric forms thereof, or mixtures of

stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

-Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents;

5 -R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

10 [21] Further preferred compounds of the present invention include compounds of claim 16 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

15 one of R^{6a} and R^{7a} is selected from:
-C₃-C₆ cycloalkyl, each such C₃-C₆ cycloalkyl
optionally substituted with 1-3 substituents
independently selected at each occurrence from
20 C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl,

25 -aryl,
-heteroaryl or
-heterocyclyl,
and the other of R^{6a} and R^{7a} is unsubstituted C₁-C₄ alkyl.

30 [22] Further preferred compounds of the present invention include compounds of claim 16 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein

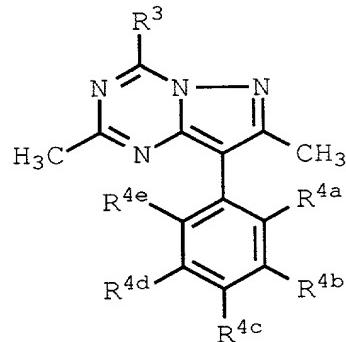
35 -R^{6a} and R^{7a} are independently selected from:

- R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl, each such C₁-C₁₀ alkyl optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
- 5 halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.
- 10 [23] Further preferred compounds of the present invention include compounds of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R¹ is independently selected at each occurrence from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl, C₂-C₁₂ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.
- 15 [24] Further preferred compounds of the present invention include compounds of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R² is selected independently at each occurrence from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -NR⁶R⁷, C₁-C₄ haloalkyl, -OR⁷.
- 20 [25] Further preferred compounds of the present invention include compounds of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R⁴ is independently selected at each occurrence from: H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆

- cycloalkyl, C₄-C₁₂ cycloalkylalkyl, halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, COR⁷, OR⁷, S(O)_n(C₁-C₁₀ alkyl), where each such C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₆ cycloalkyl and C₄-C₁₂ cycloalkylalkyl are
- 5 optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₄ alkyl, NR⁶R⁷, COR⁷ OR⁷, CO₂R⁷ and where R⁷ in SONR⁷ is C₁-C₁₀ alkyl.
- 10 [26] Further preferred compounds of the present invention include compounds of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R⁴ is
- 15 independently selected at each occurrence from: H, C₁-C₁₀ alkyl, C₁-C₄ alkoxy, halo, CN and -NR⁶R⁷.

[27] Further preferred compounds of the present invention include compounds of Formula (50)

20



FORMULA (50)

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and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and

pharmaceutically acceptable salt forms thereof, selected from the group consisting of:

- 5 a compound of Formula (50) wherein R³ is -NHCH(n-Pr)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -NHCH(Et)(n-Bu), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NHCH(CH₂OEt)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -N(Me)(Ph), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(Et)(n-Pr), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

- 5 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

10 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is -OEt, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is -N(CH₂CN)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is -NHCH(Me)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is -OCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

45 a compound of Formula (50) wherein R³ is -N(n-Pr)(CH₂cPr), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

50 a compound of Formula (50) wherein R³ is -NHCH(Me)(CH₂N(Me)₂), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -
 $\text{N}(\text{cPr})(\text{CH}_2\text{CH}_2\text{CN})$, R^{4a} is Me, R^{4b} is H, R^{4c} is Me,
R^{4d} is H and R^{4e} is H;

- 5 a compound of Formula (50) wherein R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

10 a compound of Formula (50) wherein R³ is -N(n-Bu)(CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

20 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

25 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

40 a compound of Formula (50) wherein R³ is -NHCH(CH₂CH₂OMe)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is morpholino, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

5 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

a compound of Formula (50) wherein R^3 is $-NHCH(Et)_2$, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R^3 is $-NH(c-Pr)$, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂,
R^{4a} is CN, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

a compound of Formula (50) wherein R³ is -N(c-
Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d}
is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is -NCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 is Br, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is -
 NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me,
 R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is
 H;
- 10 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c}
 is Me, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d}
 is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d}
 is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is (S)-
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c}
 is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -
 NH(CH₂OMe)(CH₂-iPr), R^{4a} is Me, R^{4b} is H, R^{4c} is
 Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is NMe₂, R^{4d} is H and R^{4e}
 is H;

- RECORDED BY
S. D. GOLDBECK
- a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe) (n-Pr), R^{4a} is Me, R^{4b} is H, R^{4c} is Me,
 R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OEt) (Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me,
 R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe) (CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 is NMe₂, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is
 Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is
 H;
- 30 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is
 Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is
 Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is NMe₂, R^{4d} is H and R^{4e} is
 H;

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- a compound of Formula (50) wherein R³ is (S)-
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 is Me, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 is Me, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is (S)-
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d}
 is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NH(Et)(CH₂CN),
 R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is
 H;
- 30 a compound of Formula (50) wherein R³ is -
 N(CH₂CH₂OMe)(CH₂CH₂OH), R^{4a} is Cl, R^{4b} is H, R^{4c} is
 Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
 R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 40 a compound of Formula (50) wherein R³ is -N(CH₂c-Pr) (n-
 Pr), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and
 R^{4e} is H;

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- a compound of Formula (50) wherein R³ is -N(c-Pr)
 $(\text{CH}_2\text{CH}_2\text{CN})$, R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d}
 is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -NHCH(Et)₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 10 a compound of Formula (50) wherein R³ is -
 NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is
 Cl, R^{4b} is H, R^{4c} is CN, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d}
 is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NHCH(CH₂OH)₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is
 H; and
- 30 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
 1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and
 R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is cyclobutyl-
 amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 40 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

- 5 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

10 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

15 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is
 Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
 Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is N(Me)propargyl,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

30 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
 H and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;
- 35 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;

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- a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is
 Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
 Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is
 Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)propargyl,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 20 a compound of Formula (50) wherein R³ is N(Et)propargyl,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 25 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
 Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;

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- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 5 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is
OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)propargyl,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 25 a compound of Formula (50) wherein R³ is N(Et)propargyl,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

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- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH₂CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
 is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
 H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 25 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
 is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 30 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
 1-yl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
 and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is cyclobutyl-
 amino, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
 and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 45 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;

- a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;
- 5 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;
- 10 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is
OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)propargyl,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;
- 30 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is
OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is
Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
is H;

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- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
 and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH₂CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
 is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
 is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 35 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
 1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and
 R^{4e} is Me;
- 40 a compound of Formula (50) wherein R³ is cyclobutyl-
 amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is Me;

- a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 5 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 25 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 30 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 40 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;

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- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 25 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 30 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

- a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

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- a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

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- a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
OMe;
- 5 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and
R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is cyclobutyl-
amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 20 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 25 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 30 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 35 a compound of Formula (50) wherein R³ is N(Me)cPr, R^{4a} is
Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

- a compound of Formula (50) wherein R³ is N(Me)propargyl,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 5 a compound of Formula (50) wherein R³ is N(Et)propargyl,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 10 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- 35 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is OMe;

a compound of Formula (50) wherein R^3 is $NHCH(Et)_2$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is OMe ;

- 5 a compound of Formula (50) wherein R^3 is $N(Et)_2$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is OMe ;

10 a compound of Formula (50) wherein R^3 is $NHCH(Et)_2$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H ;

15 a compound of Formula (50) wherein R^3 is 2-ethylpiperid-1-yl, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H ;

20 a compound of Formula (50) wherein R^3 is cyclobutyl-amino, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H ;

25 a compound of Formula (50) wherein R^3 is $N(Et)CH_2CH=CH_2$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H ;

30 a compound of Formula (50) wherein R^3 is $N(Me)CH_2cPr$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H ;

35 a compound of Formula (50) wherein R^3 is $N(Et)CH_2cPr$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H ;

40 a compound of Formula (50) wherein R^3 is $N(Pr)CH_2cPr$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H ;

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- a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R^3 is $NHCH(cPr)_2$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H ;

5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

a compound of Formula (50) wherein R^3 is $NHCH(Et)_2$, R^{4a}
 is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R^3 is $N(Et)_2$, R^{4a} is Cl , R^{4b} is H , R^{4c} is OMe , R^{4d} is H and R^{4e} is H .

15 a compound of Formula (50) wherein R^3 is $NHCH(Et)_2$, R^{4a}
 is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

20 a compound of Formula (50) wherein R^3 is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;

a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
 is H;

- a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is
Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 10 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is
Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Me)propargyl,
15 15 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- a compound of Formula (50) wherein R³ is
NH(CH(CH₃)CH(CH₃)CH₃), R^{4a} is Cl, R^{4b} is H, R^{4c} is
20 20 OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
F and R^{4e} is H;
- 25 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 30 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
35 35 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F
40 40 and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is
 $\text{NH}(\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3)$, R^{4a} is Cl, R^{4b} is F, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 15 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H.
- 20 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 25 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe
and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is cyclobutyl-
amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe
and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;

a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

- 5 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

10 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is
 Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
 Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is N(Me)propargyl,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

25 a compound of Formula (50) wherein R³ is
 NH(CH(CH₃)CH(CH₃)CH₃), R^{4a} is Cl, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is OMe and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
 F and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

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- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
 is H;

- 5 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

10 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

15 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is
 Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
 Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is N(Me)propargyl,
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

30 a compound of Formula (50) wherein R³ is
 NH(CH(CH₃)CH(CH₃)CH₃), R^{4a} is Br, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is OMe and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is
 F and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

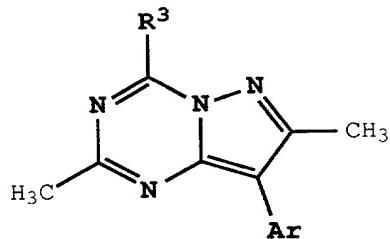
a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
 is H;

- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH₂CH₃), R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H.
- 30 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH(CH₃)CH₃), R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 45 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH₂CH₃), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H; and
- 30 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H.

[28] Further preferred compounds of the present invention include compounds of claim 4 of Formula (60)



and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and

- 5 pharmaceutically acceptable salt forms thereof, selected from the group consisting of:

a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- 10 a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- 15 a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- 20 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- 25 a compound of Formula (60) wherein R³ is N(Me)cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6-dimethylamino-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
6-dimethylamino-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Et)propargyl,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
15 NH(CH(CH₃)CH(CH₃)CH₃), Ar is 6-dimethylamino-4-
methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-
20 yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃), Ar is 6-dimethylamino-4-
methylpyrid-3-yl;

5

a compound of Formula (60) wherein R³ is NHCH(cPr)₂ Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar is
6-dimethylamino-4-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is 2-ethylpiperid-
1-yl, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

20

a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

30 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar
is 6-dimethylamino-4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
6-dimethylamino-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6-dimethylamino-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH(CH₃)CH₃), Ar is 6-dimethylamino-4-
methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-
yl;
- 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 35 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 40 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃), Ar is 6-dimethylamino-4-
methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
is 6-dimethylamino-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar
is 6-dimethylamino-4-methylpyrid-3-yl.
- 20 a compound of Formula (60) wherein R³ is 2-ethylpiperid-
1-yl, Ar is 6- methoxy -4-methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 6- methoxy -4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- 35 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar
is 6- methoxy -4-methylpyrid-3-yl;
- 40 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- 45 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
6- methoxy -4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6- methoxy -4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Et)propargyl,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
15 NHCH(CH₃)CH(CH₃)CH₃, Ar is 6- methoxy -4-
methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6- methoxy -4-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
25 Ar is 6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 6- methoxy -4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH₂CH₃, Ar is 6-methoxy-4-methylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is NHCH(cPr)₂ Ar
is 6-methoxy-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-methoxy-4-methylpyrid-3-yl;

10 a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar is
6-methoxy-4-methylpyrid-3-yl;

15 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
6-methoxy-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 4-methoxy-6-methylpyrid-3-yl;

20 a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 4-methoxy-6-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂,
Ar is 4-methoxy-6-methylpyrid-3-yl;

25 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar
is 4-methoxy-6-methylpyrid-3-yl;

30 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar
is 4-methoxy-6-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Me)cPr, Ar is
4-methoxy-6-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
4-methoxy-6-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 4-methoxy-6-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, Ar is 4-methoxy-6-methylpyrid-
3-yl;
- 15 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
Ar is 4-methoxy-6-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
25 Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃), Ar is 4-methoxy-6-methylpyrid-3-
yl;

- a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
is 4-methoxy-6-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar
is 6- methoxy -4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
4- methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is 2-ethylpiperid-
15 1-yl, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 4,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar
is 4,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
30 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Et Ar is
4,6-dimethylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
4,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Et)propargyl,
Ar is 4,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
15 CH₂CH=CH₂, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
Ar is 4,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
Ar is 4,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
30 NHCH(CH₃)CH₂CH₃, Ar is 4,6-dimethylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar is 4,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 4,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar is
4,6-dimethylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is 2-ethylpiperid-
1-yl, Ar is 2,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is cyclobutyl-
amino, Ar is 2,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂,
Ar is 2,6-dimethylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar
is Ar is 2,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar
is Ar is 2,6-dimethylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
2,6-dimethylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
2,6-dimethylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
2,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH(CH₃)CH₃, Ar is 2,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
15 Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
Ar is 2,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, Ar is 2,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃, Ar is 2,6-dimethyl pyrid-3-yl;
- a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
30 is 2,6-dimethyl pyrid-3-yl;

a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 2,6-dimethylpyrid-3-yl;

5 a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar
is 2,6-dimethyl-pyrid-3-yl; and

10 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
2,6-dimethyl-pyrid-3-yl.

15 [29] Further preferred compounds of the present invention include compounds of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof, wherein said compound is selected from the group consisting of:

- 20 4-((2-butyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
25 4-((2-butyl)amino)-2,7-dimethyl-8-(2,5-di methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
30 4-((3-pentyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
4-((3-pentyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
4-(N-cyclopropylmethyl-N-propylamino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

- 4-(N-cyclopropylmethyl-N-propylamino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 5 4-(N-allyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 10 4-(N-allyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 15 4-(diallylamino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 20 4-(diallylamino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine; and
- 25 4-(N-ethyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine.
- [30] The present invention further provides for pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claims 6, 11, 16, 27, 28 and 29.
- [31] The present invention further provides for a method of treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression,

Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in mammals comprising administering to the mammal a therapeutically effective amount of a compound of claim claims 4, 6, 11, 16, 27, 28 and 29.

15 .

Many compounds of this invention have one or more asymmetric centers or planes. Unless otherwise indicated, all chiral (enantiomeric and diastereomeric) and racemic forms are included in the present invention. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds, and all such stable isomers are contemplated in the present invention. The compounds may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. All chiral, (enantiomeric and diastereomeric) and racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomer form is specifically indicated.

The term "alkyl" includes both branched and straight-chain alkyl having the specified number of carbon atoms. Commonly used abbreviations have the following meanings: Me is methyl, Et is ethyl, Pr is propyl, Bu is butyl. As is conventional, in a chemical

structure drawing, a straight single bond attached to an atom at one end but with no atom designation at the other end indicates the presence of a methyl group at the unattached end of the bond. The prefix "n" means
5 a straight chain alkyl. The prefix "c" means a cycloalkyl. The prefix "(S)" means the S enantiomer and the prefix "(R)" means the R enantiomer. Alkenyl" includes hydrocarbon chains of either a straight or branched configuration and one or more unsaturated
10 carbon-carbon bonds which may occur in any stable point along the chain, such as ethenyl, propenyl, and the like. "Alkynyl" includes hydrocarbon chains of either a straight or branched configuration and one or more triple carbon-carbon bonds which may occur in any
15 stable point along the chain, such as ethynyl, propynyl and the like. "Haloalkyl" is intended to include both branched and straight-chain alkyl having the specified number of carbon atoms, substituted with 1 or more halogen; "alkoxy" represents an alkyl group
20 of indicated number of carbon atoms attached through an oxygen bridge; "cycloalkyl" is intended to include saturated ring groups, including mono-, bi- or poly-cyclic ring systems, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and so forth. "Halo" or
25 "halogen" includes fluoro, chloro, bromo, and iodo.

The term "substituted", as used herein, means that one or more hydrogen on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is
30 not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced.

Combinations of substituents and/or variables are permissible only if such combinations result in
35 stable compounds. By "stable compound" or "stable structure" is meant a compound that is sufficiently

robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

- The term "appropriate amino acid protecting group" means any group known in the art of organic synthesis for the protection of amine or carboxylic acid groups. Such amine protecting groups include those listed in Greene and Wuts, "Protective Groups in Organic Synthesis" John Wiley & Sons, New York (1991) and "The Peptides: Analysis, Synthesis, Biology, Vol. 3, Academic Press, New York (1981), the disclosure of which is hereby incorporated by reference. Any amine protecting group known in the art can be used.
- Examples of amine protecting groups include, but are not limited to, the following: 1) acyl types such as formyl, trifluoroacetyl, phthalyl, and p-toluenesulfonyl; 2) aromatic carbamate types such as benzyloxycarbonyl (Cbz) and substituted benzyloxycarbonyls, 1-(p-biphenyl)-1-methylethoxycarbonyl, and 9-fluorenylmethyloxycarbonyl (Fmoc); 3) aliphatic carbamate types such as tert-butyloxycarbonyl (Boc), ethoxycarbonyl, diisopropylmethoxycarbonyl, and allyloxycarbonyl; 4) cyclic alkyl carbamate types such as cyclopentyloxycarbonyl and adamantlyloxycarbonyl; 5) alkyl types such as triphenylmethyl and benzyl; 6) trialkylsilane such as trimethylsilane; and 7) thiol containing types such as phenylthiocarbonyl and dithiasuccinoyl.
- The term "pharmaceutically acceptable salts" includes acid or base salts of the compounds of Formulae (1) and (2). Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like.

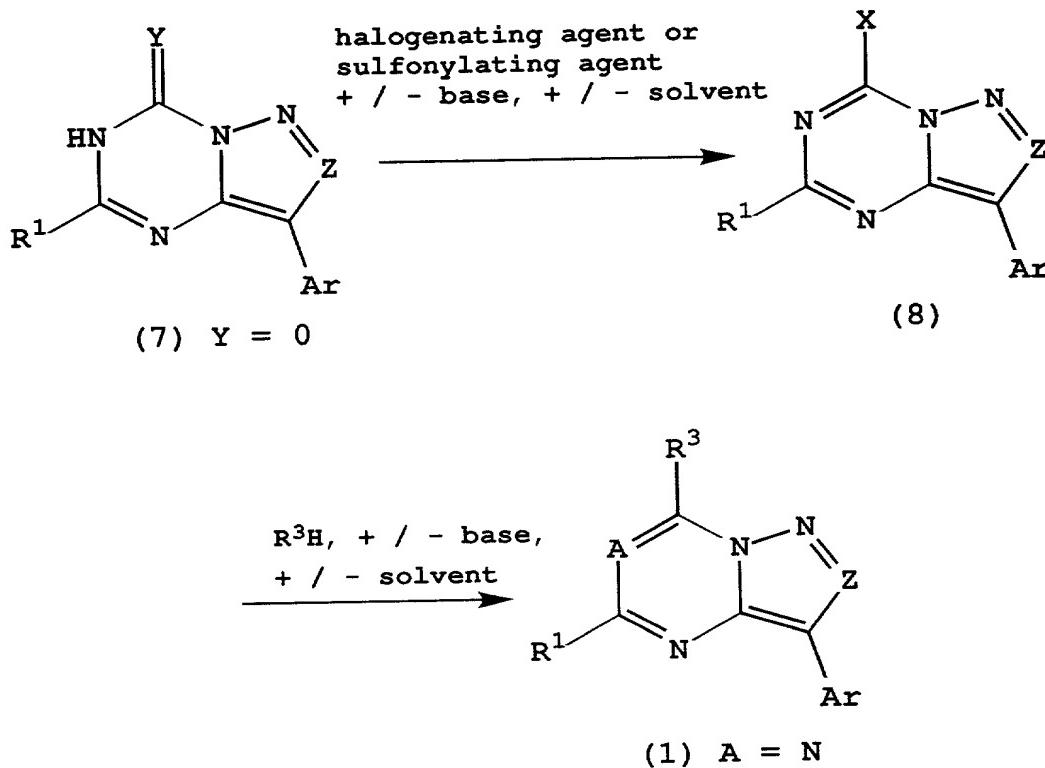
Pharmaceutically acceptable salts of the compounds of the invention can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid 5 in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in Remington's Pharmaceutical Sciences, 17th ed., Mack 10 Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

"Prodrugs" are considered to be any covalently bonded carriers which release the active parent drug 15 of formula (I) or (II) *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of the compounds of formula (I) and (II) are prepared by modifying functional groups present in the compounds in such a way that the modifications are cleaved, 20 either in routine manipulation or *in vivo*, to the parent compounds. Prodrugs include compounds wherein hydroxy, amine, or sulphhydryl groups are bonded to any group that, when administered to a mammalian subject, cleaves to form a free hydroxyl, amino, or sulphhydryl 25 group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of formulas (I) and (II); and the like.

The term "therapeutically effective amount" of a 30 compound of this invention means an amount effective to antagonize abnormal level of CRF or treat the symptoms of affective disorder, anxiety or depression in a host.

Some compounds of Formula (1) may be prepared from intermediate compounds of Formula (7), using the procedures outlined in Scheme 1:

SCHEME 1



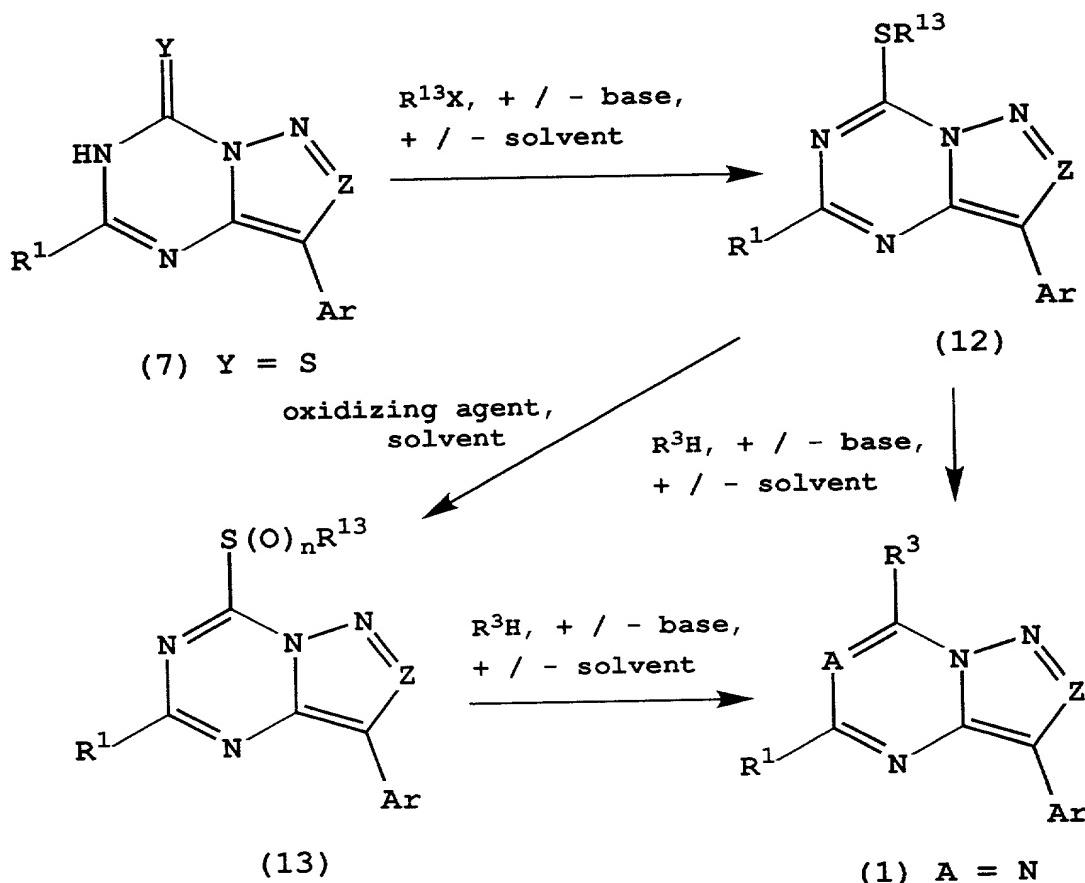
- 5 Compounds of Formula (7) (where Y is O) may be treated
 with a halogenating agent or sulfonylating agent in the
 presence or absence of a base in the presence or absence
 of an inert solvent at reaction temperatures ranging
 10 from -80°C to 250°C to give products of Formula (8)
 (where X is halogen, alkanesulfonyloxy, arylsulfonyloxy
 or haloalkane-sulfonyloxy). Halogenating agents
 include, but are not limited to, SOCl₂, POCl₃, PCl₃,
 PCl₅, POBr₃, PBr₃ or PBr₅. Sulfonylating agents include,
 15 but are not limited to, alkanesulfonyl halides or
 anhydrides (such as methanesulfonyl chloride or
 methanesulfonic acid anhydride), arylsulfonyl halides or

anhydrides (such as p-toluenesulfonyl chloride or anhydride) or haloalkylsulfonyl halides or anhydrides (preferably trifluoromethanesulfonic anhydride). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium diisopropylamide), alkali metal bis(trimethylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -20°C to 100°C.

Compounds of Formula (8) may be reacted with compounds of Formula R³H (where R³ is defined as above except R³ is not SH, COR⁷, CO₂R⁷, aryl or heteroaryl) in the presence or absence of a base in the presence or absence of an inert solvent at reaction temperatures ranging from -80 to 250°C to generate compounds of Formula (1). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably

- REF ID: A650950
- lithium di-isopropylamide), alkali metal carbonates,
alkali metal bicarbonates, alkali metal
bis(trialkylsilyl)amides (preferably sodium
bis(trimethylsilyl)amide), trialkyl amines (preferably
5 N,N-di-isopropyl-N-ethyl amine) or aromatic amines
(preferably pyridine). Inert solvents may include, but
are not limited to, alkyl alcohols (1 to 8 carbons,
preferably methanol or ethanol), lower alkanenitriles (1
to 6 carbons, preferably acetonitrile), dialkyl ethers
10 (preferably diethyl ether), cyclic ethers (preferably
tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides
(preferably dimethylformamide), N,N-dialkylacetamides
(preferably dimethylacetamide), cyclic amides
(preferably N-methylpyrrolidin-2-one), dialkylsulfoxides
15 (preferably dimethylsulfoxide), aromatic hydrocarbons
(preferably benzene or toluene) or haloalkanes of 1 to
10 carbons and 1 to 10 halogens (preferably
dichloromethane). Preferred reaction temperatures range
from 0°C to 140°C.
- 20 Scheme 2 delineates the procedures for converting
intermediate compounds of Formula (7) (where Y is S) to
some compounds of Formula (1).

SCHEME 2



Compounds of Formula (7) (where Y is S) may be treated with an alkylating agent R¹³X (where R¹³ is defined as above, except R¹³ is not aryl or heteroaryl) in the presence or absence of a base in the presence or absence of an inert solvent at reaction temperatures ranging from -80°C to 250°C. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal hydroxides, alkali metal bis(trialkylsilyl)amides (preferably sodium

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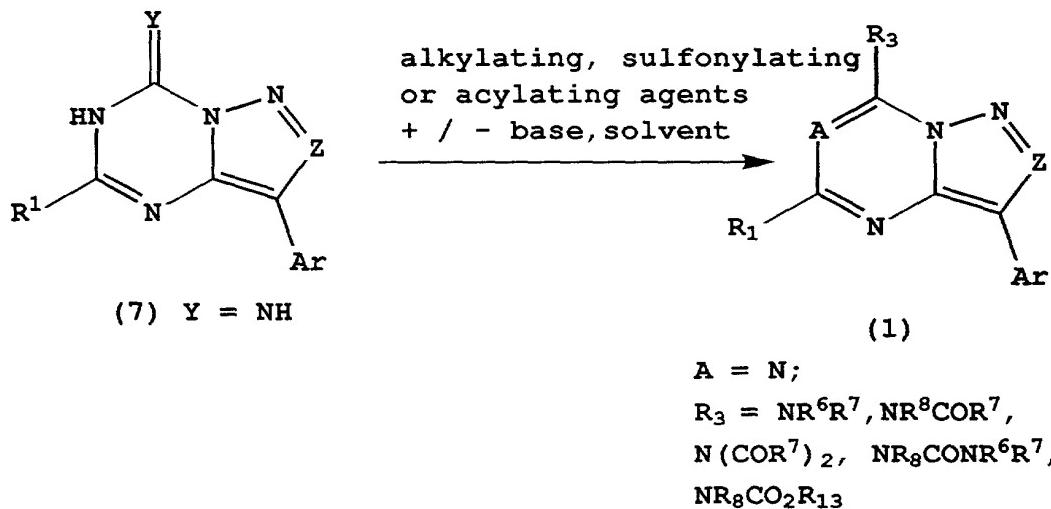
bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -80°C to 100°C.

Compounds of Formula (12) (Formula (1) where R³ is SR¹³) may then be reacted with compounds of Formula R³H to give compounds of Formula (1), using the same conditions and reagents as were used for the conversion of compounds of Formula (8) to compounds of Formula (1) as outlined for Scheme 1 above. Alternatively, compounds of Formula (12) (Formula (1) where R³ is SR¹³) may be oxidized to compounds of Formula (13) (Formula (1) where R³ is S(O)_nR¹³, n is 1,2) by treatment with an oxidizing agent in the presence of an inert solvent at temperatures ranging from -80°C to 250°C. Oxidizing agents include, but are not limited to, hydrogen peroxide, alkane or aryl peracids (preferably peracetic acid or m-chloro-perbenzoic acid), dioxirane, oxone, or sodium periodate. Inert solvents may include, but are not limited to, alkanones (3 to 10 carbons, preferably acetone), water, alkyl alcohols (1 to 6 carbons), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens

(preferably dichloromethane) or combinations thereof. The choices of oxidant and solvent are known to those skilled in the art (cf. Uemura, S., Oxidation of Sulfur, Selenium and Tellurium, in Comprehensive Organic Synthesis, Trost, B.M. ed., (Elmsford, NY: Pergamon Press, 1991), 7, 762-769). Preferred reaction temperatures range from -20°C to 100°C. Compounds of Formula (13) (Formula (1) where R³ is S(O)_nR¹³, n is 1,2) may then be reacted with compounds of Formula R³H to give compounds of Formula (1), using the same conditions and reagents as were used for the conversion of compounds of Formula (8) to compounds of Formula (1) as outlined for Scheme (1) above.

Compounds of Formula (1), where R³ may be -NR⁸COR⁷, -N(COR⁷)₂, -NR⁸CONR⁶R⁷, -NR⁸CO₂R¹³, -NR⁶R⁷, -NR⁸SO₂R⁷, may be prepared from compounds of Formula (7), where Y is NH, by the procedures depicted in Scheme 3.

SCHEME 3



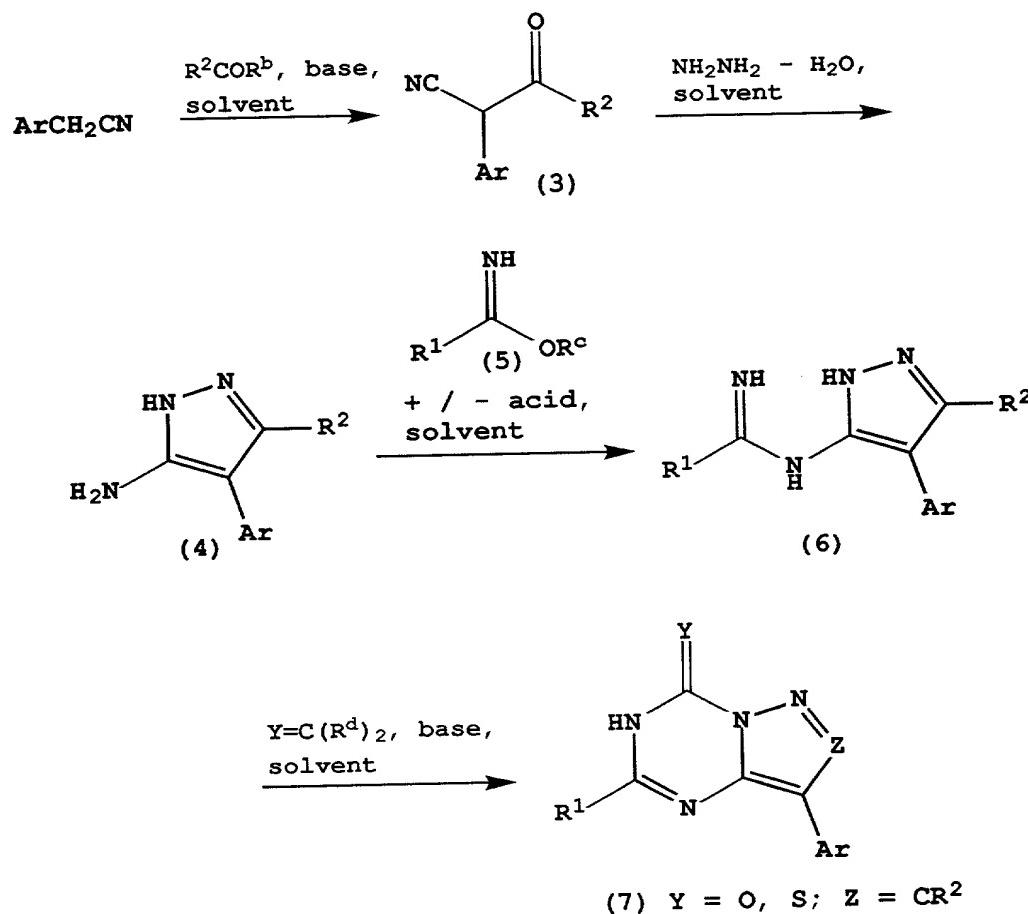
- 20 Reaction of compounds of Formula (7), where Y is NH, with alkylating agents, sulfonylating agents or acylating agents or sequential reactions with combinations thereof, in the presence or absence of a

base in an inert solvent at reaction temperatures ranging from -80°C to 250°C may afford compounds of Formula (1), where R³ may be -NR⁸COR⁷, -N(COR⁷)₂, -NR⁸CONR⁶R⁷, -NR⁸CO₂R¹³, -NR⁶R⁷, -NR⁸SO₂R⁷. Alkylating agents may include, but are not limited to, C₁-C₁₀ alkyl-halides, -tosylates, -mesylates or -triflates; C₁-C₁₀ haloalkyl(1 - 10 halogens)-halides, -tosylates, -mesylates or -triflates; C₂-C₈ alkoxyalkyl-halides, -tosylates, -mesylates or -triflates; C₃-C₆ cycloalkyl-halides, -tosylates, -mesylates or -triflates; C₄-C₁₂ cycloalkylalkyl-halides, -tosylates, -mesylates or -triflates; aryl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates or -triflates; heteroaryl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates or -triflates; or heterocyclyl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates or -triflates. Acylating agents may include, but are not limited to, C₁-C₁₀ alkanoyl halides or anhydrides, C₁-C₁₀ haloalkanoyl halides or anhydrides with 1 - 10 halogens, C₂-C₈ alkoxyalkanoyl halides or anhydrides, C₃-C₆ cycloalkanoyl halides or anhydrides, C₄-C₁₂ cycloalkylalkanoyl halides or anhydrides, aroyl halides or anhydrides, aryl(C₁-C₄) alkanoyl halides or anhydrides, heteroaroyl halides or anhydrides, heteroaryl(C₁-C₄) alkanoyl halides or anhydrides, heterocyclylcarboxylic acid halides or anhydrides or heterocyclyl(C₁-C₄) alkanoyl halides or anhydrides. Sulfonating agents include, but are not limited to, C₁-C₁₀ alkylsulfonyl halides or anhydrides, C₁-C₁₀ haloalkylsulfonyl halides or anhydrides with 1 - 10 halogens, C₂-C₈ alkoxyalkylsulfonyl halides or anhydrides, C₃-C₆ cycloalkylsulfonyl halides or anhydrides, C₄-C₁₂ cycloalkylalkylsulfonyl halides or anhydrides, arylsulfonyl halides or anhydrides, aryl(C₁-C₄ alkyl)-, heteroarylsulfonyl halides or anhydrides, heteroaryl(C₁-C₄ alkyl)sulfonyl halides or anhydrides, heterocyclylsulfonyl halides or anhydrides or

2025
heterocyclyl (C₁-C₄ alkyl) sulfonyl halides or anhydrides. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium diisopropylamide), alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from 0°C to 100°C.

Scheme 4 delineates procedures, which may be employed to prepare intermediate compounds of Formula (7), where Y is O, S and Z is CR².

SCHEME 4



Compounds of the formula ArCH₂CN are reacted with compounds of the formula R²COR^b, where R² is defined above and R^b is halogen, cyano, lower alkoxy (1 to 6 carbons) or lower alkanoyloxy (1 to 6 carbons), in the presence of a base in an inert solvent at reaction temperatures ranging from -78°C to 200°C to afford compounds of Formula (3). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal

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dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal hydroxides, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably 5 N,N-di-isopropyl-N-ethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), water, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), 15 dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from 0°C to 100°C.

Compounds of Formula (3) may be treated with hydrazine-hydrate in the presence of an inert solvent at 20 temperatures ranging from 0°C to 200°C, preferably 70°C to 150°C, to produce compounds of Formula (4). Inert solvents may include, but are not limited to, water, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, 25 preferably acetonitrile), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides 30 (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Compounds of Formula (4) may be reacted with compounds of Formula (5) (where R^c is alkyl (1-6 carbons)) in the presence or absence of an acid in the presence of an inert solvent at 35 temperatures ranging from 0°C to 200°C to produce compounds of Formula (6). Acids may include, but are

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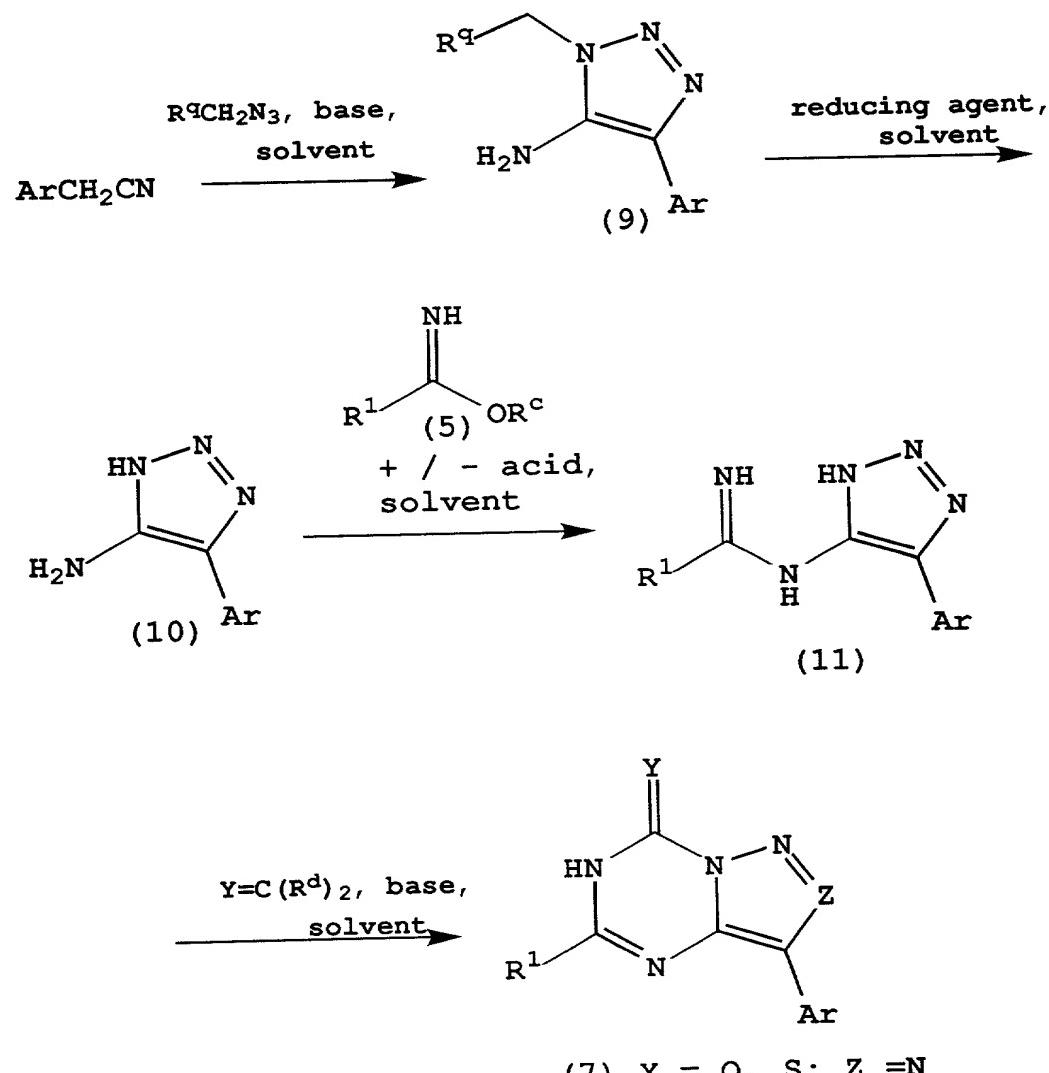
not limited to alkanoic acids of 2 to 10 carbons (preferably acetic acid), haloalkanoic acids (2 - 10 carbons, 1-10 halogens, such as trifluoroacetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or 5 benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Stoichiometric or catalytic amounts of such acids may be used. Inert solvents may include, but are not limited to, water, 10 alkanenitriles (1 to 6 carbons, preferably acetonitrile), halocarbons of 1 to 6 carbons and 1 to 6 halogens (preferably dichloromethane or chloroform), alkyl alcohols of 1 to 10 carbons (preferably ethanol), dialkyl ethers (4 to 12 carbons, preferably diethyl 15 ether or di-isopropylether) or cyclic ethers such as dioxan or tetrahydrofuran. Preferred temperatures range from ambient temperature to 100°C.

Compounds of Formula (6) may be converted to intermediate compounds of Formula (7) by treatment with 20 compounds C=Y(R^d)₂ (where Y is O or S and R^d is halogen (preferably chlorine), alkoxy (1 to 4 carbons) or alkylthio (1 to 4 carbons)) in the presence or absence of a base in an inert solvent at reaction temperatures from -50°C to 200°C. Bases may include, but are not 25 limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkali metal carbonates, alkali metal hydroxides, trialkyl amines (preferably N,N-di- 30 isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), cyclic ethers (preferably tetrahydrofuran 35 or 1,4-dioxane), N,N-dialkylformamides (preferably

dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably 5 benzene or toluene). Preferred temperatures are 0°C to 150°C.

Intermediate compounds of Formula (7), where Z is N, may be synthesized according the methods outlined in Scheme 5.

SCHEME 5



Compounds of ArCH_2CN are reacted with compounds of Formula $\text{R}^q\text{CH}_2\text{N}_3$ (where R^q is a phenyl group optionally substituted by H, alkyl (1 to 6 carbons) or alkoxy (1 to 6 carbons) in the presence or absence of a base in an inert solvent at temperatures ranging from 0°C to 200°C to generate compounds of Formula (9). Bases may include, but are not limited to, alkali metal hydrides

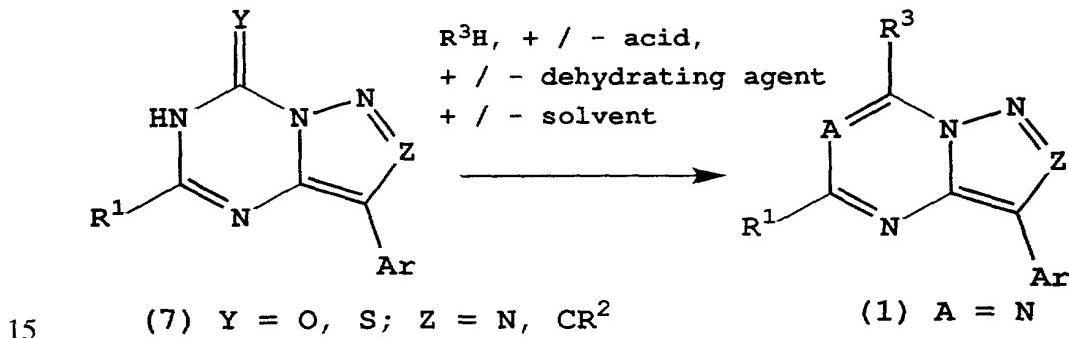
(preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide, sodium ethoxide or potassium t-butoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal hydroxides, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine).
5 di-isopropylamide), alkali metal carbonates, alkali metal hydroxides, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine).
10 Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably
15 tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons
20 (preferably benzene or toluene). Preferred reaction temperatures range from ambient temperature to 100°C.

Compounds of Formula (9) may be treated with a reducing agent in an inert solvent at -100°C to 100°C to afford products of Formula (10). Reducing agents
25 include, but are not limited to, (a) hydrogen gas in combination with noble metal catalysts such as Pd-on-carbon, PtO₂, Pt-on-carbon, Rh-on-alumina or Raney nickel, (b) alkali metals (preferably sodium) in combination with liquid ammonia or (c) ceric ammonium nitrate. Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), water, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably
30 tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides
35 (preferably dimethylacetamide), N,N-dialkylacetamides

(preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). The preferred reaction 5 temperatures are -50°C to 60°C. Compounds of Formula (9) are then converted to compounds of Formula (7) (where Z is N) via intermediates of Formula (11) using the reagents and reaction conditions outlined in Scheme 10 4 for the conversion of compounds of Formula (4) to compounds of Formula (7) (where Z is CR²).

Compounds of Formula (1) may also be prepared from compounds of Formula (7) (where Y is O, S and Z is defined above) as outlined in Scheme 6:

SCHEME 6



15 (7) Y = O, S; Z = N, CR²

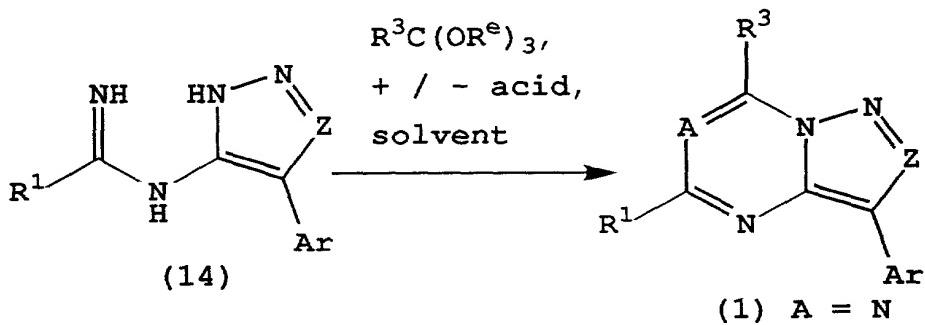
(1) $A = N$

Compounds of Formula (7) may be reacted with compounds of Formula R³H in the presence of a dehydrating agent in an inert solvent at reaction temperatures ranging from 0°C to 250°C. Dehydrating agents include, but are not limited to, P₂O₅, molecular sieves or inorganic or organic acids. Acids may include, but are not limited to alkanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Inert solvents may include, but are not limited to,

alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably glyme or diglyme), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or halocarbons of 1 to 10 carbons and 1 to 10 halogens (preferably chloroform). Preferred reaction temperatures range from ambient temperature to 150°C.

Some compounds of Formula (1) (where A is N) may also be prepared by the methods shown in Scheme 7:

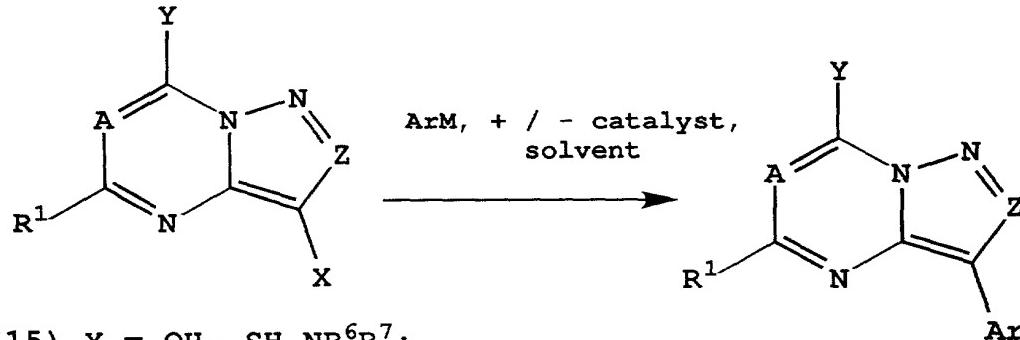
SCHEME 7



Intermediate compounds of Formula (14), where Z is defined above, may be reacted with compounds of Formula R³C(OR⁹)₃, where R⁹ may be alkyl (1 to 6 carbons) in the presence or absence of an acid in an inert solvent at temperatures ranging from 0°C to 250°C. Acids may include, but are not limited to alcanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Stoichiometric or

- catalytic amounts of such acids may be used. Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from 50°C to 150°C.
- 5 Intermediate compounds of Formula (7) may also be synthesized by the reactions displayed in Scheme 8.

SCHEME 8



- Compounds of Formula (15), (where Y is OH, SH, NR⁶R⁷; Z is defined above, X is Br, Cl, I, O₃SCF₃ or B(OR''')₂ and R''' is H or alkyl (1 to 6 carbons)) may be reacted with a compound of Formula ArM (where M is halogen, alkali metal, ZnCl, ZnBr, ZnI, MgBr, MgCl, MgI, CeCl₂, CeBr₂ or copper halides) in the presence or absence of an organometallic catalyst in the presence or absence of a
- 20
25

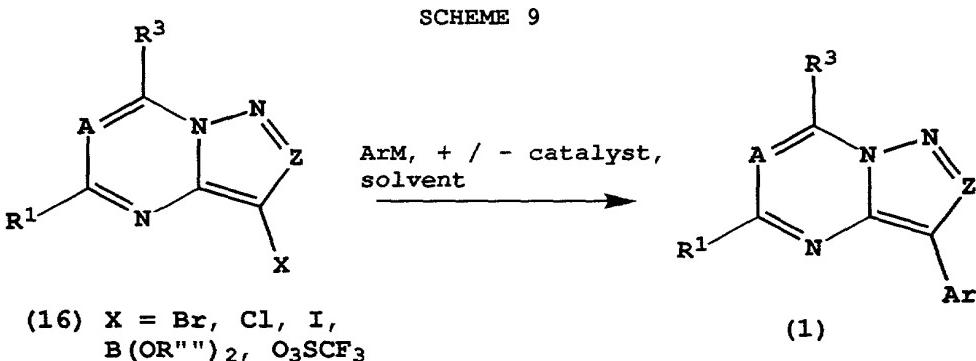
base in an inert solvents at temperatures ranging from -100°C to 200°C. Those skilled in the art will recognize that the reagents ArM may be generated in situ.

Organometallic catalysts include, but are not limited
5 to, palladium phosphine complexes (such as Pd(PPh₃)₄), palladium halides or alkanoates (such as PdCl₂(PPh₃)₂ or Pd(OAc)₂) or nickel complexes (such as NiCl₂(PPh₃)₂).

Bases may include, but are not limited to, alkali metal
10 carbonates or trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine). Inert solvents may include, but are not limited to, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or water. Preferred reaction temperatures range from -80°C
15 to 100°C.

The choices of M and X are known to those skilled in the art (cf. Imamoto, T., Organocerium Reagents in Comprehensive Organic Synthesis, Trost, B.M. ed., (Elmsford, NY: Pergamon Press, 1991), 1, 231-250; Knochel, P., Organozinc, Organocadmium and Organomercury Reagents in Comprehensive Organic Synthesis, Trost, B.M. ed., (Elmsford, NY: Pergamon Press, 1991), 1, 211-230; Knight, D.W., Coupling Reactions between sp² Carbon Centers, in Comprehensive Organic Synthesis, Trost, B.M.
20 ed., (Elmsford, NY: Pergamon Press, 1991), 3, 481-520).

Compounds of Formula (1) may also be prepared using the methods shown in Scheme 9.



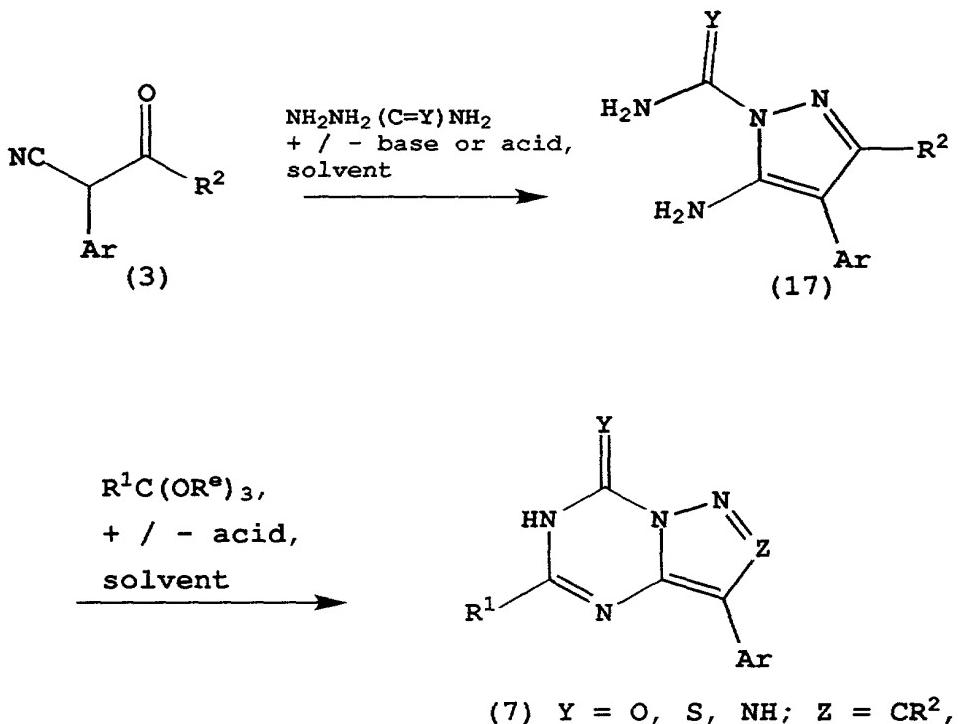
Compounds of Formula (16), where A, Z, R¹ and R³ are defined above and X is Br, Cl, I, O₃SCF₃ or B(OR'')₂ and R'' is H or alkyl (1 to 6 carbons)) may be reacted with a compound of Formula ArM (where M is halogen, alkali metal, ZnCl, ZnBr, ZnI, MgBr, MgCl, MgI, CeCl₂, CeBr₂ or copper halides) in the presence or absence of an organometallic catalyst in the presence or absence of a base in an inert solvents at temperatures ranging from -100°C to 200°C. Those skilled in the art will recognize that the reagents ArM may be generated in situ (see the above references in Comprehensive Organic Synthesis). Organometallic catalysts include, but are not limited to, palladium phosphine complexes (such as Pd(PPh₃)₄), palladium halides or alkanoates (such as PdCl₂(PPh₃)₂ or Pd(OAc)₂) or nickel complexes (such as NiCl₂(PPh₃)₂). Bases may include, but are not limited to, alkali metal carbonates or trialkyl amines (preferably N,N-diisopropyl-N-ethyl amine or triethylamine). Inert solvents may include, but are not limited to, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or

water. Preferred reaction temperatures range from -80°C to 100°C.

Intermediate compounds of Formula (7) (where Y is O, S, NH, Z is CR² and R¹, R² and Ar are defined as above)

5 may be prepared as illustrated in Scheme 10.

SCHEME 10



Compounds of Formula (3) may be reacted with compounds of Formula $\text{H}_2\text{NNH}(\text{C}=\text{Y})\text{NH}_2$, where Y is O, S or NH, in the presence or absence of a base or acid in an inert solvent at temperatures from 0°C to 250°C to produce compounds of Formula (17). Acids may include, but are not limited to alkanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Stoichiometric or catalytic amounts

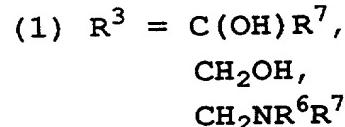
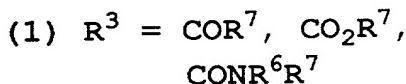
of such acids may be used. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 6 carbons), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane).

Preferred reaction temperatures range from 0°C to 150°C. Compounds of Formula (17) may then be reacted with compounds of Formula $R^3C(OR^e)_3$, where R^e may be alkyl (1 to 6 carbons) in the presence or absence of an acid in an inert solvent at temperatures ranging from 0°C to 250°C. Acids may include, but are not limited to alkanoic acids of 2 to 10 carbons (preferably acetic acid), arylsulfonic acids (preferably p-toluenesulfonic acid or benzenesulfonic acid), alkanesulfonic acids of 1 to 10 carbons (preferably methanesulfonic acid), hydrochloric acid, sulfuric acid or phosphoric acid. Stoichiometric or catalytic amounts of such acids may be used. Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably

- acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane).
- 5 Preferred reaction temperatures range from 50°C to 10 150°C.

In Scheme 11, the procedures which may be used to convert compounds of Formula (1), where R³ is COR⁷, CO₂R⁷, NR⁸COR⁷ and CONR⁶R⁷, to other compounds of Formula 15 (1), where R³ is CH(OH)R⁷, CH₂OH, NR⁸CH₂R⁷ and CH₂NR⁶R⁷ by treatment with a reducing agent in an inert solvent at temperatures ranging from -80°C to 250°C.

SCHEME 11



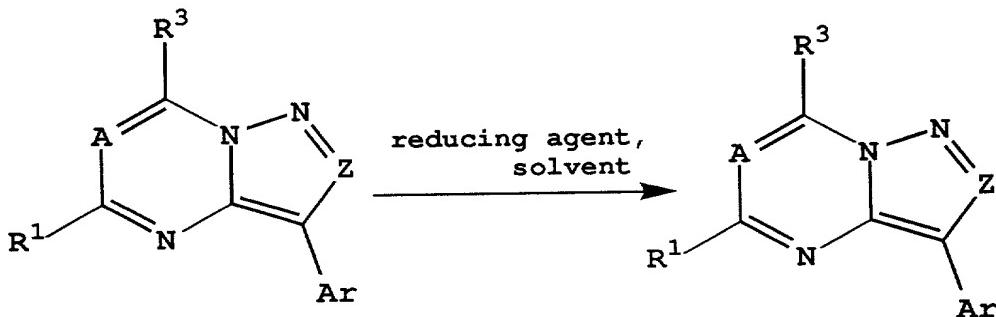
- 20 Reducing agents include, but are not limited to, alkali metal or alkaline earth metal borohydrides (preferably lithium or sodium borohydride), borane, dialkylboranes (such as di-isoamylborane), alkali metal aluminum hydrides (preferably lithium aluminum hydride), alkali metal (trialkoxy)aluminum hydrides, or dialkyl aluminum 25

hydrides (such as di-isobutylaluminum hydride). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 6 carbons), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably

- 5 tetrahydrofuran or 1,4-dioxane), aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from -80°C to 100°C.

In Scheme 12, the procedures are shown which may be used to convert compounds of Formula (1), where R³ is COR⁷ or CO₂R⁷, to other compounds of Formula (1), where R³ is C(OH)(R⁷)₂ by treatment with a reagent of Formula R⁷M in an inert solvent at temperatures ranging from -80°C to 250°C.

SCHEME 12

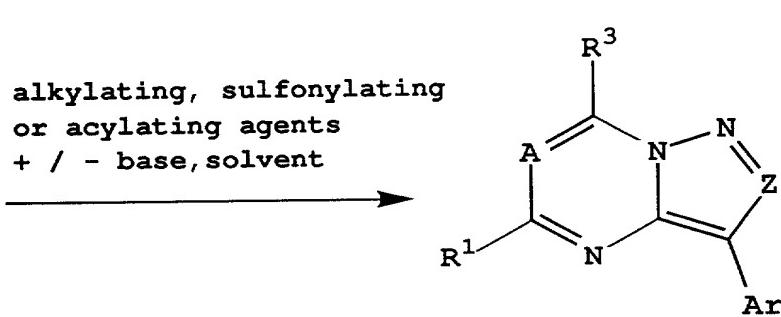
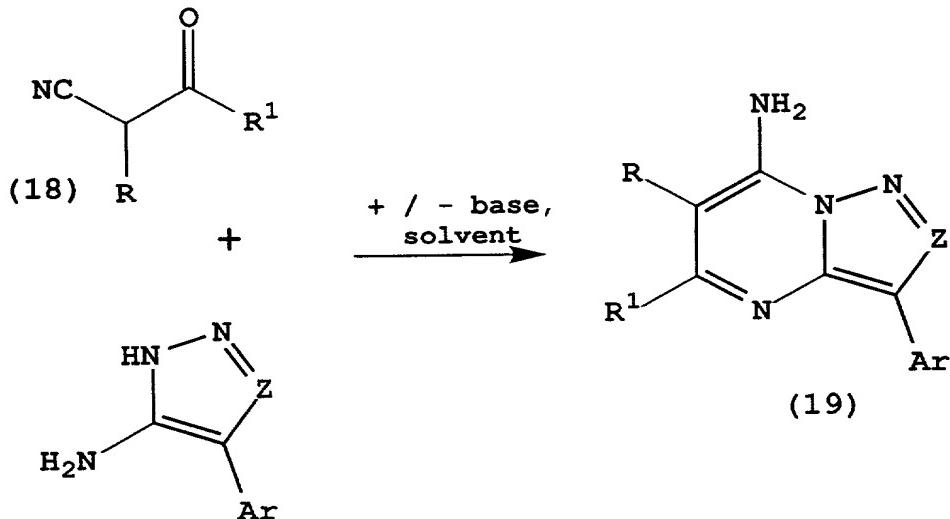


- 15 (1) R³ = COR⁷, CO₂R⁷, (1) R³ = C(OH)(R⁷)₂

M is halogen, alkali metal, ZnCl, ZnBr, ZnI, MgBr, MgCl, MgI, CeCl₂, CeBr₂ or copper halides. Inert solvents may include, but are not limited to, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from -80°C to 100°C.

- 20 Compounds of Formula (1), where R³ may be -NR⁸COR⁷, -N(COR⁷)₂, -NR⁸CONR⁶R⁷, -NR⁸CO₂R¹³, -NR⁶R⁷, -NR⁸SO₂R⁷,
25 may be synthesized as depicted in Scheme 13.

SCHEME 13



$\text{A} = \text{CR}$
 $\text{R}_3 = \text{NR}^6\text{R}^7, \text{NR}^8\text{COR}^7,$
 $\text{N}(\text{COR}^7)_2,$
 $\text{NR}_8\text{CONR}^6\text{R}^7,$
 $\text{NR}_8\text{CO}_2\text{R}_{13}$

Reaction of compounds of Formula (18), where R and R¹ are defined above, with compounds of Formula (4) or (10) in the presence or absence of base in an inert solvent may produce compounds of Formula (19) at temperatures

ranging from -50°C to 250°C. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from 0°C to 100°C.

Compounds of Formula (19) may then be reacted with alkylating agents, sulfonylating agents or acylating agents or sequential reactions with combinations thereof, in the presence or absence of a base in an inert solvent at reaction temperatures ranging from - 80°C to 250°C may afford compounds of Formula (1), where R³ may be -NR⁸COR⁷, -N(COR⁷)₂, -NR⁸CONR⁶R⁷, -NR⁸CO₂R¹³, - NR⁶R⁷, -NR⁸SO₂R⁷. Alkylating agents may include, but are not limited to, C₁-C₁₀ alkyl -halides, -tosylates, -mesylates or -triflates; C₁-C₁₀ haloalkyl(1 - 10 halogens)-halides, -tosylates, -mesylates or -triflates; C₂-C₈ alkoxyalkyl-halides, -tosylates, -mesylates or - triflates; C₃-C₆ cycloalkyl-halides, -tosylates, -

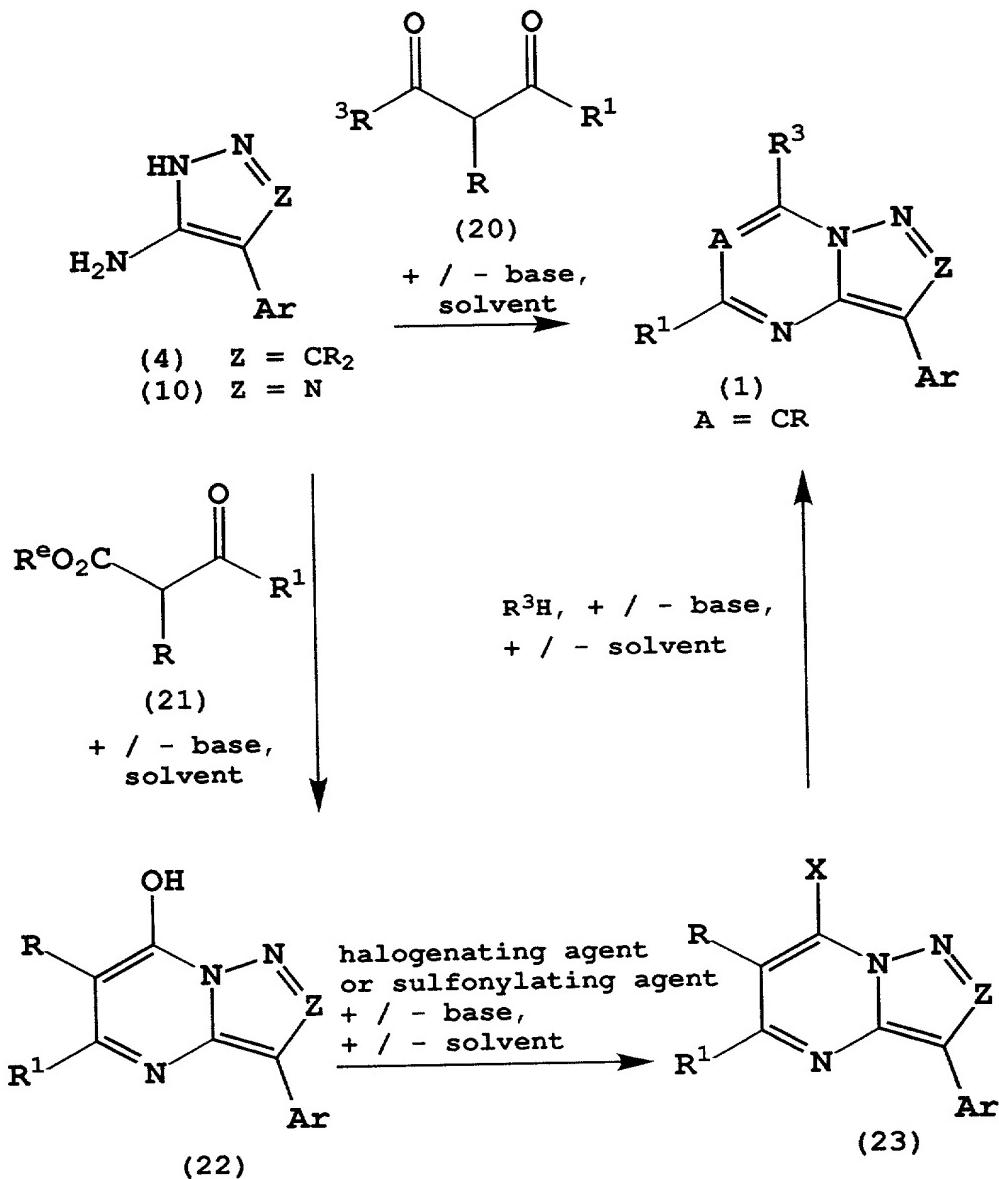
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mesylates or -triflates; C₄-C₁₂ cycloalkylalkyl-halides,
-tosylates, -mesylates or -triflates; aryl(C₁-C₄ alkyl)-
halides, -tosylates, -mesylates or -triflates;
heteroaryl(C₁-C₄ alkyl)-halides, -tosylates, -mesylates
5 or -triflates; or heterocyclyl(C₁-C₄ alkyl)-halides, -
tosylates, -mesylates or -triflates. Acylating agents
may include, but are not limited to, C₁-C₁₀ alkanoyl
halides or anhydrides, C₁-C₁₀ haloalkanoyl halides or
anhydrides with 1 - 10 halogens, C₂-C₈ alkoxyalkanoyl
10 halides or anhydrides, C₃-C₆ cycloalkanoyl halides or
anhydrides, C₄-C₁₂ cycloalkylalkanoyl halides or
anhydrides, aroyl halides or anhydrides, aryl(C₁-C₄)
alkanoyl halides or anhydrides, heteroaroyl halides or
anhydrides, heteroaryl(C₁-C₄) alkanoyl halides or
15 anhydrides, heterocyclylcarboxylic acid halides or
anhydrides or heterocyclyl(C₁-C₄) alkanoyl halides or
anhydrides. Sulfonating agents include, but are not
limited to, C₁-C₁₀ alkylsulfonyl halides or anhydrides,
C₁-C₁₀ haloalkylsulfonyl halides or anhydrides with 1 -
20 10 halogens, C₂-C₈ alkoxyalkylsulfonyl halides or
anhydrides, C₃-C₆ cycloalkylsulfonyl halides or
anhydrides, C₄-C₁₂ cycloalkylalkylsulfonyl halides or
anhydrides, arylsulfonyl halides or anhydrides, aryl(C₁-
C₄ alkyl)-, heteroarylsulfonyl halides or anhydrides,
25 heteroaryl(C₁-C₄ alkyl)sulfonyl halides or anhydrides,
heterocyclylsulfonyl halides or anhydrides or
heterocyclyl(C₁-C₄ alkyl)sulfonyl halides or anhydrides.
Bases may include, but are not limited to, alkali metal
30 hydrides (preferably sodium hydride), alkali metal
alkoxides (1 to 6 carbons) (preferably sodium methoxide
or sodium ethoxide), alkaline earth metal hydrides,
alkali metal dialkylamides (preferably lithium di-
isopropylamide), alkali metal carbonates, alkali metal
bis(trialkylsilyl)amides (preferably sodium
35 bis(trimethylsilyl)amide), trialkyl amines (preferably

- di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from 0°C to 100°C.
- Compounds of Formula (1), where A is CR and R is defined above, may be synthesized by the methods depicted in Scheme 14.

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SCHEME 14



Compounds of Formula (4) or (10) may be treated with compounds of Formula (20), where R^1 and R^3 are defined above in the presence or absence of base in an inert solvent at temperatures ranging from 0°C to 250°C to give compounds of Formula (1), where A is CR and R is defined above. Bases may include, but are not limited

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to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably 5 lithium di-isopropylamide), alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not 10 limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides 15 (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction 20 temperatures range from 0°C to 100°C. Alternatively, compounds of Formula (1) where A is CR and R is defined above, may be synthesized through intermediates (22) and (23).

Compounds of Formula (4) or (10) may be treated 25 with compounds of Formula (21), where R¹ is defined above and R^e is alkyl (1 - 6 carbons), in the presence or absence of base in an inert solvent at temperatures ranging from 0°C to 250°C to give compounds of Formula (1), where A is CR and R is defined above. Bases may 30 include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), 35 alkali metal carbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium

bis(trimethylsilyl)amide), trialkyl amines (preferably di-isopropylethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably 5 methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide) or aromatic hydrocarbons (preferably benzene or toluene). Preferred reaction temperatures range from 0°C to 100°C. Compounds of 10 Formula (22) may be treated with a halogenating agent or sulfonylating agent in the presence or absence of a base in the presence or absence of an inert solvent at reaction temperatures ranging from -80°C to 250°C to give products of Formula (23) (where X is halogen, 15 20 25 30 35 alkanesulfonyloxy, arylsulfonyloxy or haloalkane-sulfonyloxy). Halogenating agents include, but are not limited to, SOCl_2 , POCl_3 , PCl_3 , PCl_5 , POBr_3 , PBr_3 or PBr_5 . Sulfonylating agents include, but are not limited to, alkanesulfonyl halides or anhydrides (such as methanesulfonyl chloride or methanesulfonic acid anhydride), arylsulfonyl halides or anhydrides (such as p-toluenesulfonyl chloride or anhydride) or haloalkylsulfonyl halides or anhydrides (preferably trifluoromethanesulfonic anhydride). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably

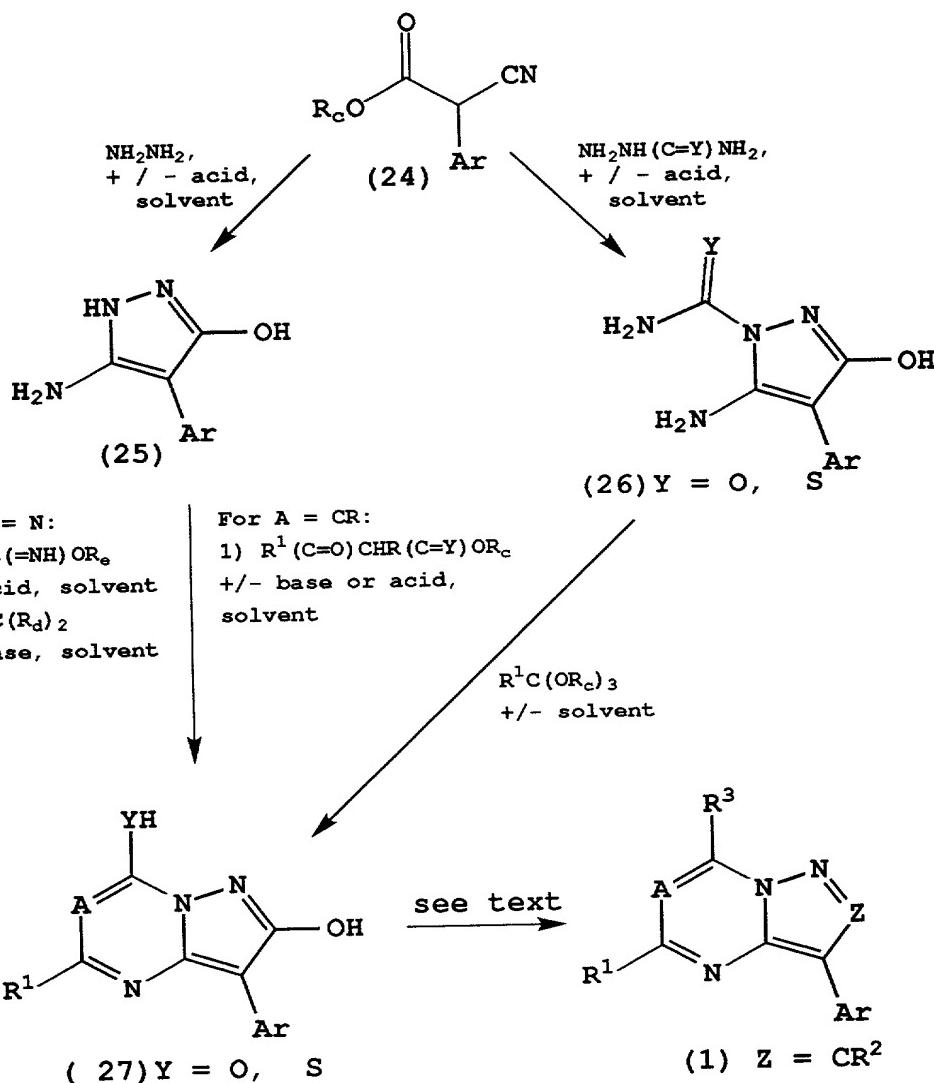
N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from -20°C to 100°C.

Compounds of Formula (23) may be reacted with compounds of Formula R³H (where R³ is defined as above except R³ is not SH, COR⁷, CO₂R⁷, aryl or heteroaryl) in the presence or absence of a base in the presence or absence of an inert solvent at reaction temperatures ranging from -80°C to 250°C to generate compounds of Formula (1). Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal carbonates, alkali metal bicarbonates, alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably N,N-di-isopropyl-N-ethyl amine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, alkyl alcohols (1 to 8 carbons, preferably methanol or ethanol), lower alkanenitriles (1 to 6 carbons, preferably acetonitrile), dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably

- tetrahydrofuran or 1,4-dioxane), N,N-dialkylformamides (preferably dimethylformamide), N,N-dialkylacetamides (preferably dimethylacetamide), cyclic amides (preferably N-methylpyrrolidin-2-one), dialkylsulfoxides 5 (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes of 1 to 10 carbons and 1 to 10 halogens (preferably dichloromethane). Preferred reaction temperatures range from 0°C to 140°C.
- 10 Some compounds of Formula (1) may also be prepared using the methods shown in Scheme 15.

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SCHEME 15



- A compound of Formula (24) (R_c is a lower alkyl group and Ar is defined as above) may be reacted with 5 hydrazine in the presence or absence of an inert solvent to afford an intermediate of Formula (25), where Ar is defined as above. The conditions employed are similar to those used for the preparation of intermediate of Formula (4) from compound of Formula (3) in Scheme 4.
- 10 Compounds of Formula (25), where A is N, may be reacted with reagents of the formula $\text{R}^1\text{C}(=\text{NH})\text{OR}_e$, where R^1 is defined above and R_e is a lower alkyl group) in the

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presence or absence of an acid in an inert solvent, followed by reaction with a compound of formula $YisC(R_d)_2$ (where Y is O or S and R_d is halogen (preferably chlorine), alkoxy (1 to 4 carbons) or 5 alkylthio (1 to 4 carbons)) in the presence or absence of a base in an inert solvent to give compounds of Formula (27) (where A is N and Y is O, S). The conditions for these transformations are the same as those employed for the conversions of compound of 10 Formula (4) to compound of Formula (7) in Scheme 4.

Alternatively, compounds of Formula (25), where A is CR, may be reacted with compounds of the formula $R^1(C=O)CHR(C=Y)OR_c$ (where R^1 and R are defined as above and R_c is a lower alkyl group) to give a compound of 15 Formula (27) (where A is CR) using conditions similar to those employed for the conversion of compounds of Formula (21) to compounds of Formula (22) in Scheme 14. Intermediates of Formula (27) (where Y is O) may be treated with halogenating agents or sulfonylating agents 20 in the presence or absence of a base in an inert solvent, followed by reaction with R^3H or R^2H in the presence or absence of a base in an inert solvent to give compounds of Formula (1) (where Z is CR^2).

It will be recognized by those skilled in the art 25 that various combinations of halogenating agents, sulfonylating agents, R^3H or R^2H may be used in different orders of reaction sequences in Scheme 15 to afford compounds of Formula (1). For example, in some cases, it may be desirable to react compounds with 30 stoichiometric amounts of halogenating agents or sulfonylating agents, react with R^2H (or R^3H), then repeat the reaction with halogenating agents or sulfonylating agents and react with R^3H (or R^2H) to give compounds of Formula (1). The reaction conditions and 35 reagents used for these conversions are similar to the ones employed for the conversion of intermediate

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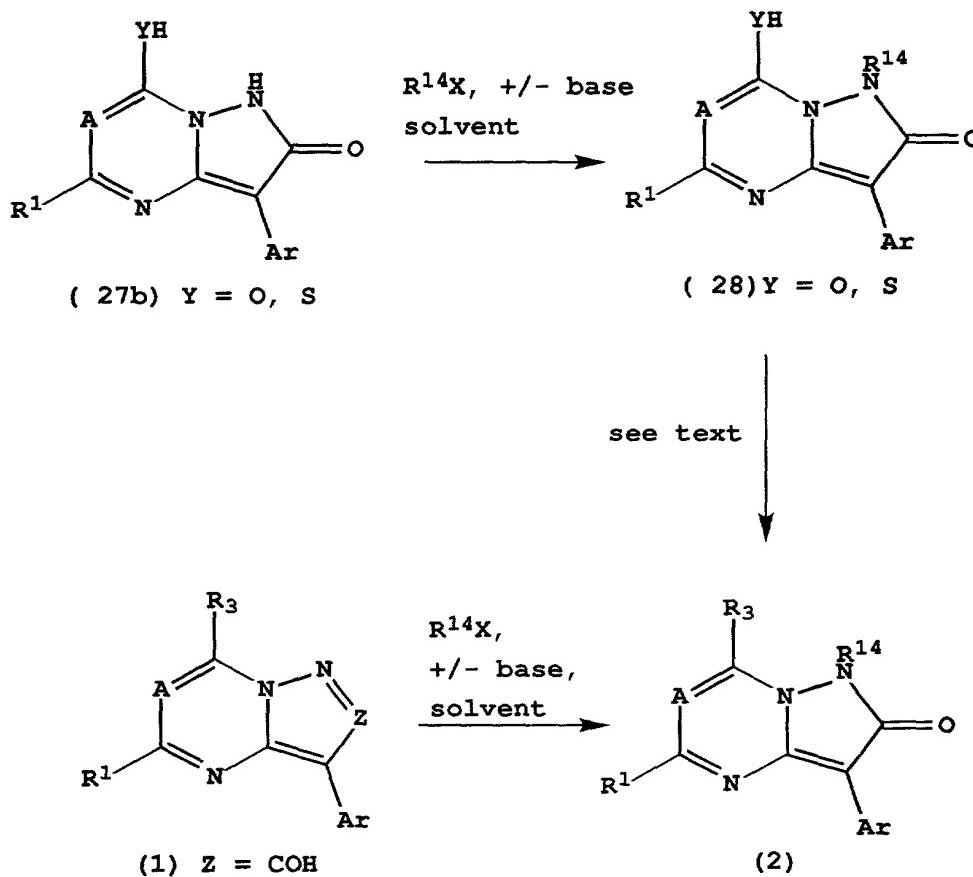
compounds of Formulae (22) to (23) to (1) in Scheme 14
(for A is CR) or the conversion of intermediate
compounds of Formulae (7) to (8) to (1) in Scheme 1
(where A is N).

- 5 Alternatively, compounds of Formula (27) (where Y
is S) may be converted to compounds of Formula (1) in
Scheme 15. Intermediate compounds of Formula (27) may
be alkylated with a compound R^fX (where R^f is lower
alkyl and X is halogen, alkanesulfonyloxy or
10 haloalkanesulfonyloxy) in an inert solvent, (then
optionally oxidized with an oxidizing agent in an inert
solvent) and then reacted with R^3H in the presence or
absence of a base in an inert solvent to give a compound
of Formula (1). The conditions and reagents employed
15 are similar to those used in the conversion of
intermediate compounds of Formulae (7) to (12) (or to
(13)) to compounds of Formula (1) in Scheme 2.

- Compounds of Formula (1) may be prepared from
compounds of Formula (24), using an alternate route as
20 depicted in Scheme 15. Compounds of Formula (24) may be
converted to compounds of Formula (27) via reaction with
compounds of formula $NH_2NH(C=NH)NH_2$ in the presence or
absence of an acid in an inert solvent, followed by
reaction with compounds $R^1C(OR_c)_3$ (where R_c is lower
25 alkyl and R^1 is defined as above), using the conditions
employed for the conversion of compounds of Formulae (3)
to (17) to (7) in Scheme 10.

Some compounds of Formula (2) may be prepared by
the methods illustrated in Scheme 16.

SCHEME 16



Compounds of Formula (27b) may be treated with various alkylating agents $R^{14}X$ (where R^{14} is defined above and X is halogen, alkanesulfonyloxy or haloalkanesulfonyloxy) in the presence or absence of a base in an inert solvent to afford structures of Formula (28). Compounds of Formula (28) (Y is O) may then be converted to compounds of Formula (2) by treatment with halogenating agents or sulfonylating agents in the presence or absence of a base in an inert solvent, followed by reaction with R^3H in the presence or absence of a base in an inert solvent to give compounds of Formula (2). The reaction conditions used for these conversions are similar to the

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ones employed for the conversion of intermediate compounds (22) to (23) to (1) in Scheme 14 (for A is CR) or the conversion of intermediate compounds of Formulae (7) to (8) to (1) in Scheme 1 (where A is N).

- 5 Alternatively, compounds of Formula (28) (Y is S) may be alkylated with a compound R^fX (where R^f is lower alkyl and X is halogen, alkanesulfonyloxy or haloalkanesulfonyloxy) in an inert solvent, (then 10 optionally oxidized with an oxidizing agent in an inert solvent) and then reacted with R^3H in the presence or absence of a base in an inert solvent to give a compound of Formula (1). The conditions and reagents employed are similar to those used in the conversion of intermediate compounds of Formulae (7) to (12) (or to 15 (13)) to compounds of Formula (1) in Scheme 2.

Compounds of Formula (1), where Z is COH, may be converted to compounds of Formula (2) as illustrated in Scheme 16. Treatment with various alkylating agents $R^{14}X$ (where R^{14} is defined above and X is halogen, 20 alkanesulfonyloxy or haloalkanesulfonyloxy) in the presence or absence of a base in an inert solvent to afford structures (2). It will be recognized by one skilled in the art that the methods used in Scheme 16 may also be used to prepare compounds of Formula (1) 25 where Z is COR⁷.

For Scheme 16, the terms "base" and "inert solvent" may have the meanings given below. Bases may include, but are not limited to, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (1 30 to 6 carbons) (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium di-isopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably 35 N,N-di-isopropyl-N-ethyl amine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents

may include, but are not limited to, lower
alkanenitriles (1 to 6 carbons, preferably
acetonitrile), dialkyl ethers (preferably diethyl
ether), cyclic ethers (preferably tetrahydrofuran or
5 1,4-dioxane), N,N-dialkylformamides (preferably
dimethylformamide), N,N-dialkylacetamides (preferably
dimethylacetamide), cyclic amides (preferably N-
methylpyrrolidin-2-one), dialkylsulfoxides (preferably
10 dimethylsulfoxide), aromatic hydrocarbons (preferably
benzene or toluene) or haloalkanes of 1 to 10 carbons
and 1 to 10 halogens (preferably dichloromethane).
Preferred reaction temperatures range from -20°C to
100°C.

15

EXAMPLES

Analytical data were recorded for the compounds
described below using the following general procedures.
20 Proton NMR spectra were recorded on an IBM-Bruker FT-NMR
(300 MHz); chemical shifts were recorded in ppm (δ) from
an internal tetramethylsilane standard in
deuterochloroform or deuterodimethylsulfoxide as
specified below. Mass spectra (MS) or high resolution
25 mass spectra (HRMS) were recorded on a Finnegan MAT 8230
spectrometer (using chemi-ionization (CI) with NH₃ as
the carrier gas or gas chromatography (GC) as specified
below) or a Hewlett Packard 5988A model spectrometer.
Melting points were recorded on a Buchi Model 510
30 melting point apparatus and are uncorrected. Boiling
points are uncorrected. All pH determinations during
workup were made with indicator paper.

Reagents were purchased from commercial sources
and, where necessary, purified prior to use according to
35 the general procedures outlined by D. Perrin and W.L.F.
Armarego, *Purification of Laboratory Chemicals*, 3rd ed.,
(New York: Pergamon Press, 1988). Chromatography was

performed on silica gel using the solvent systems indicated below. For mixed solvent systems, the volume ratios are given. Otherwise, parts and percentages are by weight.

5

The following examples are provided to describe the invention in further detail. These examples, which set forth the best mode presently contemplated for carrying out the invention, are intended to 10 illustrate and not to limit the invention.

EXAMPLE 1

Preparation of

15 2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-[1,3,5]-triazin-4(3H)-one
(Formula 7, where Y is O, R₁ is CH₃, Z is C-CH₃, Ar is 2,4-dimethylphenyl)

20 A. 1-Cyano-1-(2,4-dimethylphenyl)propan-2-one
Sodium pellets (9.8g, 0.43 mol) were added portionwise to a solution of 2,4-dimethylphenylacetonitrile (48 g, 0.33 mol) in ethyl acetate (150 mL) at ambient temperature. The reaction mixture was heated to reflux temperature and stirred for 16 hours. The resulting suspension was cooled to room temperature and filtered. The collected precipitate was washed with copious amounts of ether and then air-dried. The solid was dissolved in water and a 1N HCl solution 25 was added until the pH = 5-6. The mixture was extracted with ethyl acetate (3 X 200 mL); the combined organic layers were dried over MgSO₄ and filtered. Solvent was removed *in vacuo* to afford a white solid (45.7g, 74% yield): NMR (CDCl₃, 300 MHz):; CI-MS: 188 (M + H).
30 B. 5-Amino-4-(2,4-dimethylphenyl)-3-methylpyrazole

A mixture of 1-cyano-1-(2,4-dimethylphenyl)propan-2-one (43.8g, 0.23 mol), hydrazine-hydrate (22 mL, 0.46 mol), glacial acetic acid (45 mL, 0.78 mol) and toluene (500 mL) were stirred at reflux temperature for 18 hours
5 in an apparatus fitted with a Dean-Stark trap. The reaction mixture was cooled to ambient temperature and solvent was removed in vacuo. The residue was dissolved in 6N HCl and the resulting solution was extracted with ether three times. A concentrated ammonium hydroxide
10 solution was added to the aqueous layer until pH = 11. The resulting semi-solution was extracted three times with ethyl acetate. The combined organic layers were dried over MgSO₄ and filtered. Solvent was removed in vacuo to give a pale brown viscous oil (34.6g, 75%
15 yield): NMR (CDCl₃, 300 MHz): 7.10 (s, 1H), 7.05 (d, 2H, J=1), 2.37 (s, 3H), 2.10 (s, 3H); CI-MS: 202 (M + H).

C. 5-Acetamidino-4-(2,4-dimethylphenyl)-3-methylpyrazole, acetic acid salt
20 Ethyl acetamide hydrochloride (60g, 0.48 mol) was added quickly to a rapidly stirred mixture of potassium carbonate (69.5g, 0.50 mol), dichloromethane (120 mL) and water (350 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (2 X 120 mL). The combined organic layers were dried over MgSO₄ and filtered. Solvent was removed by simple distillation and the pot residue, a clear pale yellow liquid, (35.0 g) was used without further purification.
25 Glacial aetic acid (9.7 mL, 0.17 mol) was added to a stirred mixture of 5-amino-4-(2,4-dimethylphenyl)-3-methylpyrazole (34g, 0.17 mol), ethyl acetamide (22g, 0.25 mol) and acetonitrile (500 mL). The resulting reaction mixture was stirred at room temperature for 3 days; at the end of which time, it was concentrated in vacuo to about one-third of its original volume. The resulting suspension was filtered and the collected
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solid was washed with copious amounts of ether. The white solid was dried *in vacuo* (31.4g, 61% yield): NMR (DMSO-d₆, 300 MHz): 7.00 (s, 1H), 6.90 (dd, 2H, J=7, 1), 2.28 (s, 3H), 2.08 (s, 3H), 2.00 (s, 3H), 1.90 (s, 3H), 5 1.81 (s, 3H); CI-MS: 243 (M + H).

D. 2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-[1,3,5]-triazin-4(3H)-one

Sodium pellets (23g, 1 mol) were added portionwise 10 to ethanol (500 mL) with vigorous stirring. After all the sodium reacted, 5-acetamido-4-(2,4-dimethylphenyl)-3-methylpyrazole, acetic acid salt (31.2g, 0.1 mol) and diethyl carbonate (97 mL, 0.8 mol) were added. The resulting reaction mixture was heated 15 to reflux temperature and stirred for 18 hours. The mix was cooled to room temperature and solvent was removed in *vacuo*. The residue was dissolved in water and a 1N HCl solution was added slowly until pH = 5-6. The aqueous layer was extracted with ethyl acetate three 20 times; the combined organic layers were dried over MgSO₄ and filtered. Solvent was removed *in vacuo* to give a pale tan solid (26g, 98% yield): NMR (CDCl₃, 300 MHz): 7.15 (s, 1H), 7.09 (s, 2H), 2.45 (s, 3H), 2.39 (s, 3H), 2.30 (s, 3H); CI-MS: 269 (M + H).

25

EXAMPLE 2

Preparation of

5-methyl-3-(2,4,6-trimethylphenyl)[1,5-a]-
[1,2,3]-triazolo-[1,3,5]-triazin-7(6H)-one
30 (Formula 7, where Y is O, R₁ is CH₃, Z is N,
Ar is 2,4,6-trimethylphenyl)

A. 1-Phenylmethyl-4-(2,4,6-trimethylphenyl)-5-aminotriazole

35 A mixture of 2,4,6-trimethylbenzyl cyanide (1.0g, 6.3 mmol), benzyl azide (0.92g, 6.9 mmol) and potassium

t-butoxide (0.78g, 6.9 mmol) in tetrahydrofuran (10mL) was stirred at ambient temperature for 2.5 days. The resulting suspension was diluted with water and extracted three times with ethyl acetate. The combined 5 organic layers were dried over MgSO₄ and filtered. Solvent was removed in vacuo to give a brown oil. Trituration with ether and filtration afforded a yellow solid (1.12g, 61% yield): NMR (CDCl₃, 300 MHz): 7.60-7.30 (m, 5H), 7.30-7.20 (m, 2H), 5.50 (s, 2H), 3.18 (br s, 10 2H), 2.30 (s, 3H), 2.10 (s, 6H); CI-MS: 293 (M + H).

B. 4-(2,4,6-Trimethylphenyl)-5-aminotriazole

Sodium (500 mg, 22 mmol) was added with stirring to a mixture of liquid ammonia (30 mL) and 1-phenylmethyl-15 4-(2,4,6-trimethylphenyl)-5-aminotriazole (1.1g, 3.8 mmol). The reaction mixture was stirred until a dark green color persisted. An ammonium chloride solution (mL) was added and the mixture was stirred while warming to ambient temperature over 16 hours. The residue was 20 treated with a 1M HCl solution and filtered. The aqueous layer was basified with a concentrated ammonium hydroxide solution (pH = 9) and then extracted with ethyl acetate three times. The combined organic layers were dried over MgSO₄ and filtered. Solvent was removed 25 in vacuo to give a yellow solid (520 mg), which was homogeneous by thin layer chromatography (ethyl acetate): NMR (CDCl₃, 300 MHz): 6.97 (s, 2H), 3.68-3.50 (br.s, 2H), 2.32 (s, 3H), 2.10 (s, 6H); CI-MS: 203 (M + H).

30

C. 4-(2,4,6-Trimethylphenyl)-5-acetamidinotriazole, acetic acid salt

A mixture of 4-(2,4,6-trimethylphenyl)-5-aminotriazole (400 mg, 1.98 mmol), ethyl acetamide (35 261 mg, 3 mmol) and glacial acetic acid (0.1 mL, 1.98 mmol) in acetonitrile (6 mL) was stirred at ambient

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- temperature for 4 hours. The resulting suspension was filtered and the collected solid was washed with copious amounts of ether. Drying *in vacuo* afforded a white solid (490 mg, 82% yield): NMR (DMSO-d₆, 300 MHz): 7.90-
- 5 7.70 (br s, 0.5H), 7.50-7.20 (br. s, 0.5H), 6.90 (s, 2H), 6.90 (s, 2H), 3.50-3.10 (br s, 3H), 2.30-2.20 (br s, 3H), 2.05 (d, 1H, J = 7), 1.96 (s, 6H), 1.87 (s, 6H); CI-MS: 244 (M + H).
- 10 D. 5-methyl-3-(2,4,6-trimethylphenyl)[1,5-a]-[1,2,3]-triazolo-[1,3,5]-triazin-7(4H)-one
Sodium (368 mg, 16.2 mmol) was added with stirring to ethanol (10 mL) at room temperature. After the sodium had reacted, 4-(2,4,6-trimethylphenyl)-5-
- 15 acetamidino-triazole, acetic acid salt (490 mg, 1.6 mmol) and diethyl carbonate (1.6 mL, 13 mmol) were added. The reaction mixture was stirred at reflux temperature for 5 hours, then cooled to room temperature. The reaction mixture was diluted with
- 20 water; a 1N HCl solution was added until pH = 5-6 and three extractions with ethyl acetate were performed. The combined organic layers were dried over MgSO₄ and filtered. Solvent was removed *in vacuo* to give a yellow residue. Trituration with ether and filtration afforded
- 25 a yellow solid (300 mg, 69% yield): NMR (CDCl₃, 300 MHz): 6.98 (s, 2H), 2.55 (s, 3H), 2.35 (s, 3H), 2.10 (s, 6H); CI-MS: 270 (M + H).

EXAMPLE 3

- 30 Preparation of 4-(di(carbomethoxy)methyl)-2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-1,3,5-triazine
(Formula 1, where R³ is CH(CHCO₂CH₃)₂, R₁ is CH₃, Z is C-CH₃, Ar is 2,4-dimethylphenyl)

A. 4-chloro-2,7-dimethyl-8-(2,4-dichlorophenyl) [1,5-

a]- pyrazolotriazine

A mixture of 2,7-dimethyl-8-(2,4-dimethylphenyl) [1,5-a]

5 -pyrazolo-1,3,5-triazin-4-one (Example 1, 1.38g, 4.5 mmol), N,N-dimethylaniline (1 mL, 8 mmol) and phosphorus oxychloride (10 mL) was stirred at reflux temperature for 48 hours. The excess phosphorus oxychloride was removed *in vacuo*. The residue was poured onto ice-water, stirred briefly and extracted quickly with ethyl acetate three times. The combined organic layers were washed with ice water, then dried over MgSO₄ and filtered. Solvent was removed *in vacuo* to give a brown oil. Flash column chromatography (ethyl acetate:hexanes::1:4) gave one fraction (*R*_f = 0.5). Solvent was removed *in vacuo* to afford a yellow oil (1.0g, 68% yield): NMR (CDCl₃, 300 MHz): 7.55 (d, 1H, *J* = 1), 7.38 (dd, 1H, *J* = 7, 1), 7.30 (d, 1H, *J* = 7), 2.68 (s, 3H), 2.45 (s, 3H); CI-MS: 327 (M + H).

20

B. 4-(di(carbomethoxy)methyl)-2,7-dimethyl-8-(2,4-dimethylphenyl) [1,5-a]-pyrazolo-1,3,5-triazine

Sodium hydride (60% in oil, 80 mg, 2 mmol) was washed with hexanes twice, decanted after each washing and taken up in anhydrous tetrahydrofuran (THF, 1 mL). A solution of diethyl malonate (0.32g, 2 mmol) in THF (2 mL) was added dropwise over 5 min, during which time vigorous gas evolution ensued. A solution of 4-chloro-2,7-dimethyl-8-(2,4-dichlorophenyl) [1,5-a]-pyrazolotriazine (0.5g, 1.75 mmol) in THF (2 mL) was added and the reaction mixture was then stirred under a nitrogen atmosphere for 48 hours. The resulting suspension was poured onto water and extracted three times with ethyl acetate. The combined organic layers were washed once with brine, dried over MgSO₄ and filtered. Solvent was removed *in vacuo* to give a brown

oil. Column chromatography (ethyl acetate:hexanes::1:9) afforded, after removal of solvent *in vacuo*, a pale yellow solid ($R_f = 0.2$, 250 mg, 35% yield): mp 50–52°C; NMR (CDCl_3 , 300 MHz): 12.35 (br.s, 1H, 7.15–7.00 (m, 5 H), 4.40 (q, 2H, $J = 7$), 4.30 (q, 2H, $J = 7$), 2.4, 2.35, 2.3, 2.2, 2.1 (5 s, 12H), 1.4 (t, 3H, $J = 7$), 1.35–1.25 (m, 3H); CI-HRMS: Calcd: 411.2032, Found: 411.2023.

10

EXAMPLE 6

Preparation of 4-(1,3-dimethoxy-2-propylamino)-2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolo-1,3,5-triazine

15 (Formula 1, where R^3 is $\text{NHCH}(\text{CH}_2\text{OCH}_3)_2$, R_1 is CH_3 , Z is $\text{C}-\text{CH}_3$, Ar is 2,4-dichlorophenyl)

A. 4-chloro-2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolotriazine

20 A mixture of 2,7-dimethyl-8-(2,4-dimethylphenyl)[1,5-a]-pyrazolo-1,3,5-triazin-4-one (Example 1, 1.38g, 4.5 mmol), N,N-dimethylaniline (1 mL, 8 mmol) and phosphorus oxychloride (10 mL) was stirred at reflux temperature for 48 hours. The excess phosphorus oxychloride was removed *in vacuo*. The residue was poured onto ice-water, stirred briefly and extracted quickly with ethyl acetate three times. The combined organic layers were washed with ice water, then dried over MgSO_4 and filtered. Solvent was removed *in vacuo* to give a brown oil. Flash column chromatography (ethyl acetate:hexanes::1:4) gave one fraction ($R_f = 0.5$). Solvent was removed *in vacuo* to afford a yellow oil (1.0g, 68% yield): NMR (CDCl_3 , 300 MHz): 7.55 (d, 1H, $J = 1$), 7.38 (dd, 1H, $J = 7, 1$), 7.30 (d, 1H, $J = 7$), 2.68 (s, 3H), 2.45 (s, 3H); CI-MS: 327 (M + H).

B. 4-(1,3-dimethoxy-2-propylamino)-2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolo-1,3,5-triazine
A mixture of 4-chloro-2,7-dimethyl-8-(2,4-dichlorophenyl)[1,5-a]-pyrazolo-1,3,5-triazine (Part A,
5 570 mg, 1.74 mmol), 1,3-dimethoxypropyl-2-aminopropane (25mg, 2.08 mmol) and ethanol (10 mL) was stirred at ambient temperature for 18 hours. The reaction mixture was poured onto water (25 mL) and extracted three times with ethyl acetate. The combined organic layers were dried over MgSO₄ and filtered. Solvent was removed *in vacuo*. Column chromatography (CH₂Cl₂:CH₃OH::50:1) afforded one fraction. Removal of solvent *in vacuo* gave a solid (250 mg, 35% yield): mp 118-120°C; NMR (CDCl₃, 300 MHz): 7.50 (s, 1H), 7.28 (dd, 2H, J = 8,1),
10 6.75 (d, 1H, J = 8), 4.70-4.58 (m, 1H), 3.70-3.55 (m, 4H), 3.43 (s, 6H), 2.50 (s, 3H), 2.35 (s, 3H); CI-HRMS: Calcd: 409.1072, Found: 409.1085; Analysis Calcd. for C₁₈H₂₁Cl₂N₅O₂: C, 52.69, H, 5.17, N, 17.07, Cl, 17.28; Found: C, 52.82, H, 5.06, N, 16.77, Cl, 17.50.

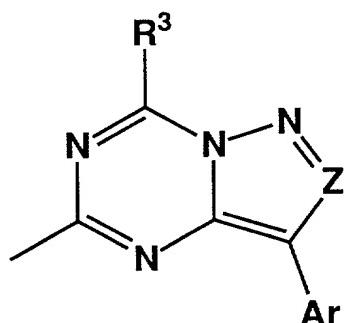
20

Using the above procedures and modifications known to one skilled in the art of organic synthesis, the following additional examples of Tables 1-4 may be prepared.

25

The examples delineated in TABLE 1 may be prepared by the methods outlined in Examples 1, 2, 3 or 6. Commonly used abbreviations are: Ph is phenyl, Pr is propyl, Me is methyl, Et is ethyl, Bu is butyl, Ex is Example.

TABLE 1



5	<u>Ex.</u>	Z	R ₃	Ar	mp (°C)
	6 ^a	C-Me	NHCH(CH ₂ OMe) ₂	2,4-Cl ₂ -Ph	118-120
	7 ^b	C-Me	NHCHPr ₂	2,4-Cl ₂ -Ph	114-116
	8 ^c	C-Me	NEtBu	2,4-Cl ₂ -Ph	oil
	9 ^d	C-Me	NPr(CH ₂ -c-C ₃ H ₅)	2,4-Cl ₂ -Ph	oil
10	10 ^e	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,4-Cl ₂ -Ph	oil
	11 ^f	C-Me	NH-3-heptyl	2,4-Cl ₂ -Ph	90-92
	12 ^g	C-Me	NHCH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph	179-181
	13 ^h	C-Me	NEt ₂	2,4-Cl ₂ -Ph	133-134
	14 ⁱ	C-Me	NHCH(CH ₂ OEt) ₂	2,4-Cl ₂ -Ph	oil
15	15 ^j	C-Me	NH-3-pentyl	2,4-Cl ₂ -Ph	139-140
	16 ^k	C-Me	NMePh	2,4-Cl ₂ -Ph	60-62
	17 ^l	C-Me	NPr ₂	2,4-Cl ₂ -Ph	oil
	18 ^m	C-Me	NH-3-hexyl	2,4-Cl ₂ -Ph	130-132
	19	C-Me	morpholino	2,4-Cl ₂ -Ph	
20	20	C-Me	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2,4-Cl ₂ -Ph	
	21	C-Me	NHCH(CH ₂ Ph)CH ₂ OMe	2,4-Cl ₂ -Ph	
	22	C-Me	NH-4-tetrahydropyranyl	2,4-Cl ₂ -Ph	
	23	C-Me	NH-cyclopentyl	2,4-Cl ₂ -Ph	
	24	C-Me	1,2,3,4-tetrahydro-	2,4-Cl ₂ -Ph	
25			isoquinolinyl		
	25	C-Me	CH ₂ - (1,2,3,4-tetrahydro- isoquinolinyl)	2,4-Cl ₂ -Ph	
	26 ⁿ	C-Me	OEt	2,4-Cl ₂ -Ph	141-143
	27	C-Me	OCH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph	

28	C-Me	OCH ₂ Ph	2,4-Cl ₂ -Ph	
29	C-Me	O-3-pentyl	2,4-Cl ₂ -Ph	
30	C-Me	SET	2,4-Cl ₂ -Ph	
31	C-Me	S(O)Et	2,4-Cl ₂ -Ph	
5	32	SO ₂ Et	2,4-Cl ₂ -Ph	
	33	CH(CO ₂ Et) ₂	2,4-Cl ₂ -Ph	
	34	C(Et)(CO ₂ Et) ₂	2,4-Cl ₂ -Ph	
	35	CH(Et)CH ₂ OH	2,4-Cl ₂ -Ph	
	36	CH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph	
10	37	CONMe ₂	2,4-Cl ₂ -Ph	
	38	COCH ₃	2,4-Cl ₂ -Ph	
	39	CH(OH)CH ₃	2,4-Cl ₂ -Ph	
	40	C(OH)Ph-3-pyridyl	2,4-Cl ₂ -Ph	
	41	Ph	2,4-Cl ₂ -Ph	
15	42	2-CF ₃ -Ph	2,4-Cl ₂ -Ph	
	43	2-Ph-Ph	2,4-Cl ₂ -Ph	
	44	3-pentyl	2,4-Cl ₂ -Ph	
	45	cyclobutyl	2,4-Cl ₂ -Ph	
	46	3-pyridyl	2,4-Cl ₂ -Ph	
20	47	CH(Et)CH ₂ CONMe ₂	2,4-Cl ₂ -Ph	
	48	CH(Et)CH ₂ CH ₂ NMe ₂	2,4-Cl ₂ -Ph	
	49 ^o	NHCH(CH ₂ OMe) ₂	2,4,6-Me ₃ -Ph	125-127
	50	NHCHPr ₂	2,4,6-Me ₃ -Ph	
	51	N <i>Et</i> Bu	2,4,6-Me ₃ -Ph	
25	52	NPr(CH ₂ -c-C ₃ H ₅)	2,4,6-Me ₃ -Ph	
	53 ^{ae}	N(CH ₂ CH ₂ OMe) ₂	2,4,6-Me ₃ -Ph	123-124
	54	NH-3-heptyl	2,4,6-Me ₃ -Ph	
	55 ^{ac}	NHCH(Et)CH ₂ OMe	2,4,6-Me ₃ -Ph	145-146
	56 ^{ah}	N <i>Et</i> ₂	2,4,6-Me ₃ -Ph	88-90
30	57ai	NHCH(CH ₂ OEt) ₂	2,4,6-Me ₃ -Ph	132-134
	58ad	NH-3-pentyl	2,4,6-Me ₃ -Ph	134-135
	59	N <i>Me</i> Ph	2,4,6-Me ₃ -Ph	
	60	NPr ₂	2,4,6-Me ₃ -Ph	
	61	NH-3-hexyl	2,4,6-Me ₃ -Ph	
35	62	morpholino	2,4,6-Me ₃ -Ph	
	63	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2,4,6-Me ₃ -Ph	

64	C-Me	NHCH(CH ₂ Ph)CH ₂ OMe	2, 4, 6-Me ₃ -Ph	
65	C-Me	NH-4-tetrahydropyranyl	2, 4, 6-Me ₃ -Ph	
66	C-Me	NH-cyclopentyl	2, 4, 6-Me ₃ -Ph	
67	C-Me	1,2,3,4-tetrahydro-	2, 4, 6-Me ₃ -Ph	
5		isoquinolinyl		
68	C-Me	CH ₂ -(1,2,3,4-tetrahydro- isoquinolinyl)	2, 4, 6-Me ₃ -Ph	
69	C-Me	OEt	2, 4, 6-Me ₃ -Ph	
70	C-Me	OCH(Et)CH ₂ OMe	2, 4, 6-Me ₃ -Ph	
10	71	C-Me	OCH ₂ Ph	2, 4, 6-Me ₃ -Ph
	72	C-Me	O-3-pentyl	2, 4, 6-Me ₃ -Ph
	73	C-Me	SEt	2, 4, 6-Me ₃ -Ph
	74	C-Me	S(O)Et	2, 4, 6-Me ₃ -Ph
	75	C-Me	SO ₂ Et	2, 4, 6-Me ₃ -Ph
15	76	C-Me	CH(CO ₂ Et) ₂	2, 4, 6-Me ₃ -Ph
	77	C-Me	C(Et)(CO ₂ Et) ₂	2, 4, 6-Me ₃ -Ph
	78	C-Me	CH(Et)CH ₂ OH	2, 4, 6-Me ₃ -Ph
	79	C-Me	CH(Et)CH ₂ OMe	2, 4, 6-Me ₃ -Ph
	80	C-Me	CONMe ₂	2, 4, 6-Me ₃ -Ph
20	81	C-Me	COCH ₃	2, 4, 6-Me ₃ -Ph
	82	C-Me	CH(OH)CH ₃	2, 4, 6-Me ₃ -Ph
	83	C-Me	C(OH)Ph-3-pyridyl	2, 4, 6-Me ₃ -Ph
	84	C-Me	Ph	2, 4, 6-Me ₃ -Ph
	85	C-Me	2-CF ₃ -Ph	2, 4, 6-Me ₃ -Ph
25	86	C-Me	2-Ph-Ph	2, 4, 6-Me ₃ -Ph
	87	C-Me	3-pentyl	2, 4, 6-Me ₃ -Ph
	88	C-Me	cyclobutyl	2, 4, 6-Me ₃ -Ph
	89	C-Me	3-pyridyl	2, 4, 6-Me ₃ -Ph
	90	C-Me	CH(Et)CH ₂ CONMe ₂	2, 4, 6-Me ₃ -Ph
30	91	C-Me	CH(Et)CH ₂ CH ₂ NMe ₂	2, 4, 6-Me ₃ -Ph
	92P	C-Me	NHCH(CH ₂ OMe) ₂	2, 4-Me ₂ -Ph
	93Q	C-Me	N(CH ₂ CH ₂ OMe) ₂	2, 4-Me ₂ -Ph
	94R	C-Me	NHCH(Et)CH ₂ OMe	2, 4-Me ₂ -Ph
	95S	C-Me	NH-3-pentyl	2, 4-Me ₂ -Ph
35	96T	C-Me	NET ₂	2, 4-Me ₂ -Ph
	97U	C-Me	N(CH ₂ CN) ₂	2, 4-Me ₂ -Ph
				44-45
				oil
				102-104
				102-104
				oil
				148-150

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98 ^v	C-Me	NHCH(Me)CH ₂ OMe	2,4-Me ₂ -Ph	102-104	
99 ^w	C-Me	OCH(Et)CH ₂ OMe	2,4-Me ₂ -Ph	oil	
100 ^x	C-Me	NPr-c-C ₃ H ₅	2,4-Me ₂ -Ph	oil	
101 ^y	C-Me	NHCH(Me)CH ₂ NMe ₂	2,4-Me ₂ -Ph	47-48	
5	102 ^z	C-Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph	117-118
	103 ^{aa}	C-Me	N(Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph	oil
	104 ^{ab}	C-Me	N(Bu)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph	oil
	105	C-Me	NHCHPr ₂	2,4-Me ₂ -Ph	
	106	C-Me	NEtBu	2,4-Me ₂ -Ph	
10	107	C-Me	NPr(CH ₂ -c-C ₃ H ₅)	2,4-Me ₂ -Ph	
	108	C-Me	NH-3-heptyl	2,4-Me ₂ -Ph	
	109	C-Me	NET ₂	2,4-Me ₂ -Ph	
	110	C-Me	NHCH(CH ₂ OEt) ₂	2,4-Me ₂ -Ph	
	111	C-Me	NH-3-pentyl	2,4-Me ₂ -Ph	
15	112	C-Me	NMePh	2,4-Me ₂ -Ph	
	113	C-Me	NPr ₂	2,4-Me ₂ -Ph	
	114	C-Me	NH-3-hexyl	2,4-Me ₂ -Ph	
	115	C-Me	morpholino	2,4-Me ₂ -Ph	
	116	C-Me	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2,4-Me ₂ -Ph	
20	117	C-Me	NHCH(CH ₂ Ph)CH ₂ OMe	2,4-Me ₂ -Ph	
	118	C-Me	NH-4-tetrahydropyranyl	2,4-Me ₂ -Ph	
	119	C-Me	NH-cyclopentyl	2,4-Me ₂ -Ph	
	120	C-Me	1,2,3,4-tetrahydro-	2,4-Me ₂ -Ph	
		isoquinolinyl			
25	121	C-Me	CH ₂ -(1,2,3,4-tetrahydro-	2,4-Me ₂ -Ph	
		isoquinolinyl)			
	122	C-Me	OEt	2,4-Me ₂ -Ph	
	123	C-Me	OCH(Et)CH ₂ OMe	2,4-Me ₂ -Ph	
	124	C-Me	OCH ₂ Ph	2,4-Me ₂ -Ph	
30	125	C-Me	O-3-pentyl	2,4-Me ₂ -Ph	
	126	C-Me	SEt	2,4-Me ₂ -Ph	
	127	C-Me	S(O)Et	2,4-Me ₂ -Ph	
	128	C-Me	SO ₂ Et	2,4-Me ₂ -Ph	
	3	C-Me	CH(CO ₂ Et) ₂	2,4-Me ₂ -Ph	50-52
35	129	C-Me	C(Et)(CO ₂ Et) ₂	2,4-Me ₂ -Ph	

130	C-Me	CH(Et)CH ₂ OH	2,4-Me ₂ -Ph	
131	C-Me	CH(Et)CH ₂ OMe	2,4-Me ₂ -Ph	
132	C-Me	CH(Et)CH ₂ OEt	2,4-Me ₂ -Ph	
133	C-Me	CONMe ₂	2,4-Me ₂ -Ph	
5	134	COCH ₃	2,4-Me ₂ -Ph	
	135	CH(OH)CH ₃	2,4-Me ₂ -Ph	
	136	C(OH)Ph-3-pyridyl	2,4-Me ₂ -Ph	
	137	Ph	2,4-Me ₂ -Ph	
	138	2-CF ₃ -Ph	2,4-Me ₂ -Ph	
	139	2-Ph-Ph	2,4-Me ₂ -Ph	
10	140	3-pentyl	2,4-Me ₂ -Ph	
	141	cyclobutyl	2,4-Me ₂ -Ph	
	142	3-pyridyl	2,4-Me ₂ -Ph	
	143	CH(Et)CH ₂ CONMe ₂	2,4-Me ₂ -Ph	
15	144	CH(Et)CH ₂ CH ₂ NMe ₂	2,4-Me ₂ -Ph	
	145 ^{bc}	NHCH(CH ₂ OMe) ₂	2-Me-4-MeO-Ph	45-46
	146 ^{bd}	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-MeO-Ph	oil
	147 ^{be}	NHCH(Et)CH ₂ OMe	2-Me-4-MeO-Ph	86-88
	148 ^{bf}	N(Pr)CH ₂ CH ₂ CN	2-Me-4-MeO-Ph	oil
20	149	OCH(Et)CH ₂ OMe	2-Me-4-MeO-Ph	
	150 ^{af}	NHCH(CH ₂ OMe) ₂	2-Br-4-MeO-Ph	88-90
	151 ^{al}	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-MeO-Ph	oil
	152 ^{ag}	NHCH(Et)CH ₂ OMe	2-Br-4-MeO-Ph	95-97
	153	N(Pr)CH ₂ CH ₂ CN	2-Br-4-MeO-Ph	
25	154	OCH(Et)CH ₂ OMe	2-Br-4-MeO-Ph	
	155	NHCH(CH ₂ OMe) ₂	2-Me-4-NMe ₂ -Ph	
	156	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-NMe ₂ -Ph	oil
	157	NHCH(Et)CH ₂ OMe	2-Me-4-NMe ₂ -Ph	
	158	N(Pr)CH ₂ CH ₂ CN	2-Me-4-NMe ₂ -Ph	
30	159	OCH(Et)CH ₂ OMe	2-Me-4-NMe ₂ -Ph	
	160	NHCH(CH ₂ OMe) ₂	2-Br-4-NMe ₂ -Ph	
	161	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-NMe ₂ -Ph	
	162	NHCH(Et)CH ₂ OMe	2-Br-4-NMe ₂ -Ph	
	163	N(Pr)CH ₂ CH ₂ CN	2-Br-4-NMe ₂ -Ph	
35	164	OCH(Et)CH ₂ OMe	2-Br-4-NMe ₂ -Ph	
	165	NHCH(CH ₂ OMe) ₂	2-Br-4-i-Pr-Ph	

166	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-i-Pr-Ph
167	C-Me	NHCH(Et)CH ₂ OMe	2-Br-4-i-Pr-Ph
168	C-Me	N(Pr)CH ₂ CH ₂ CN	2-Br-4-i-Pr-Ph
169	C-Me	OCH(Et)CH ₂ OMe	2-Br-4-i-Pr-Ph
5	170	C-Me	NHCH(CH ₂ OMe) ₂
	171	C-Me	N(CH ₂ CH ₂ OMe) ₂
	172	C-Me	NHCH(Et)CH ₂ OMe
	173	C-Me	N(Pr)CH ₂ CH ₂ CN
	174	C-Me	OCH(Et)CH ₂ OMe
10	175 ^{ar}	C-Me	NHCH(CH ₂ OMe) ₂
	176	C-Me	N(CH ₂ CH ₂ OMe) ₂
	177	C-Me	NHCH(Et)CH ₂ OMe
	178	C-Me	N(Pr)CH ₂ CH ₂ CN
	179	C-Me	OCH(Et)CH ₂ OMe
15	180	C-Me	NHCH(CH ₂ OMe) ₂
	181	C-Me	N(CH ₂ CH ₂ OMe) ₂
	182	C-Me	NHCH(CH ₂ OMe) ₂
	183	C-Me	N(CH ₂ CH ₂ OMe) ₂
	184	C-Me	NHCH(CH ₂ OMe) ₂
20	185	C-Me	N(CH ₂ CH ₂ OMe) ₂
	186	C-Me	NHCH(CH ₂ OMe) ₂
	187	C-Me	N(CH ₂ CH ₂ OMe) ₂
	188	C-Me	NHCH(CH ₂ OMe) ₂
	189	C-Me	N(CH ₂ CH ₂ OMe) ₂
25	190	C-Me	NHCH(CH ₂ OMe) ₂
	191	C-Me	N(CH ₂ CH ₂ OMe) ₂
	192	C-Me	NHCH(CH ₂ OMe) ₂
	193	C-Me	N(CH ₂ CH ₂ OMe) ₂
	194	C-Me	NHCH(CH ₂ OMe) ₂
30	195	C-Me	N(CH ₂ CH ₂ OMe) ₂
	196	C-Me	NHCH(CH ₂ OMe) ₂
	197	C-Me	N(CH ₂ CH ₂ OMe) ₂
	198	C-Me	NHCH(CH ₂ OMe) ₂
	199	C-Me	N(CH ₂ CH ₂ OMe) ₂
35	200	C-Me	NHCH(CH ₂ OMe) ₂
	201	C-Me	N(CH ₂ CH ₂ OMe) ₂
			108-109

202	C-Me	NHCH(CH ₂ OMe) ₂	4-i-Pr-2-SO ₂ Me-Ph
203	C-Me	N(CH ₂ CH ₂ OMe) ₂	4-i-Pr-2-SO ₂ Me-Ph
204	C-Me	NHCH(CH ₂ OMe) ₂	2,6-(Me)2-4-SMe-Ph
205	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,6-(Me)2-4-SMe-Ph
5	206	C-Me	NHCH(CH ₂ OMe) ₂
	207	C-Me	N(CH ₂ CH ₂ OMe) ₂
	208	C-Me	NHCH(CH ₂ OMe) ₂
	209	C-Me	N(CH ₂ CH ₂ OMe) ₂
	210	C-Me	NHCH(CH ₂ OMe) ₂
	211	C-Me	N(CH ₂ CH ₂ OMe) ₂
	212	C-Me	NHCH(CH ₂ OMe) ₂
10	213	C-Me	N(CH ₂ CH ₂ OMe) ₂
	214	C-Me	NHCH(CH ₂ OMe) ₂
	215	C-Me	N(CH ₂ CH ₂ OMe) ₂
	216	C-Me	NHCH(CH ₂ OMe) ₂
	217	C-Me	N(CH ₂ CH ₂ OMe) ₂
15	218	C-Me	NHCH(CH ₂ OMe) ₂
	219	C-Me	N(CH ₂ CH ₂ OMe) ₂
	220	C-Me	NHCH(CH ₂ OMe) ₂
	221	C-Me	N(CH ₂ CH ₂ OMe) ₂
	222	C-Me	NHCH(CH ₂ OMe) ₂
20	223	C-Me	N(CH ₂ CH ₂ OMe) ₂
	224	C-Me	NHCH(CH ₂ OMe) ₂
	225	C-Me	N(CH ₂ CH ₂ OMe) ₂
	226	H	NHCH(CH ₂ OMe) ₂
	227	H	NHCH(CH ₂ OMe) ₂
25	228	CF ₃	N(CH ₂ CH ₂ OMe) ₂
	229	CF ₃	N(CH ₂ CH ₂ OMe) ₂
	230	N	NHCH(CH ₂ OMe) ₂
	231	N	NHCHPr ₂
	232	N	NETBu
30	233	N	NPr(CH ₂ -c-C ₃ H ₅)
	234	N	N(CH ₂ CH ₂ OMe) ₂
	235	N	NH-3-heptyl
	236	N	NHCH(Et)CH ₂ OMe
	237	N	NET ₂

	238	N	NHCH(CH ₂ OEt) ₂	2, 4, 6-Me ₃ -Ph
	239	N	NH-3-pentyl	2, 4, 6-Me ₃ -Ph
	240	N	NMePh	2, 4, 6-Me ₃ -Ph
	241	N	NPr ₂	2, 4, 6-Me ₃ -Ph
5	242	N	NH-3-hexyl	2, 4, 6-Me ₃ -Ph
	243	N	morpholino	2, 4, 6-Me ₃ -Ph
	244	N	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2, 4, 6-Me ₃ -Ph
	245	N	NHCH(CH ₂ Ph)CH ₂ OMe	2, 4, 6-Me ₃ -Ph
	246	N	NH-4-tetrahydropyranyl	2, 4, 6-Me ₃ -Ph
	10	247	NH-cyclopentyl	2, 4, 6-Me ₃ -Ph
	248	N	1,2,3,4-tetrahydro- isoquinolinyl	2, 4, 6-Me ₃ -Ph
	249	N	CH ₂ -(1,2,3,4-tetrahydro- isoquinolinyl)	2, 4, 6-Me ₃ -Ph
15	250	N	OEt	2, 4, 6-Me ₃ -Ph
	251	N	OCH(Et)CH ₂ OMe	2, 4, 6-Me ₃ -Ph
	252	N	OCH ₂ Ph	2, 4, 6-Me ₃ -Ph
	253	N	O-3-pentyl	2, 4, 6-Me ₃ -Ph
	254	N	SEt	2, 4, 6-Me ₃ -Ph
20	255	N	S(O)Et	2, 4, 6-Me ₃ -Ph
	256	N	SO ₂ Et	2, 4, 6-Me ₃ -Ph
	257	N	CH(CO ₂ Et) ₂	2, 4, 6-Me ₃ -Ph
	258	N	C(Et)(CO ₂ Et) ₂	2, 4, 6-Me ₃ -Ph
	259	N	CH(Et)CH ₂ OH	2, 4, 6-Me ₃ -Ph
25	260	N	CH(Et)CH ₂ OMe	2, 4, 6-Me ₃ -Ph
	261	N	CONMe ₂	2, 4, 6-Me ₃ -Ph
	262	N	COCH ₃	2, 4, 6-Me ₃ -Ph
	263	N	CH(OH)CH ₃	2, 4, 6-Me ₃ -Ph
	264	N	C(OH)Ph-3-pyridyl	2, 4, 6-Me ₃ -Ph
30	265	N	Ph	2, 4, 6-Me ₃ -Ph
	266	N	2-CF ₃ -Ph	2, 4, 6-Me ₃ -Ph
	267	N	2-Ph-Ph	2, 4, 6-Me ₃ -Ph
	268	N	3-pentyl	2, 4, 6-Me ₃ -Ph
	269	N	cyclobutyl	2, 4, 6-Me ₃ -Ph
35	270	N	3-pyridyl	2, 4, 6-Me ₃ -Ph
	271	N	CH(Et)CH ₂ CONMe ₂	2, 4, 6-Me ₃ -Ph

272	N	CH(Et)CH ₂ CH ₂ NMe ₂	2, 4, 6-Me ₃ -Ph	
273	N	NHCH(CH ₂ OMe) ₂	2, 4-Me ₂ -Ph	
274	N	NHCHPr ₂	2, 4-Me ₂ -Ph	
275	N	NETBu	2, 4-Me ₂ -Ph	
5	276	NPr(CH ₂ -c-C ₃ H ₅)	2, 4-Me ₂ -Ph	
	277	N(CH ₂ CH ₂ OMe) ₂	2, 4-Me ₂ -Ph	
	278	NH-3-heptyl	2, 4-Me ₂ -Ph	
	279	NHCH(Et)CH ₂ OMe	2, 4-Me ₂ -Ph	
	280	NET ₂	2, 4-Me ₂ -Ph	
10	281	NHCH(CH ₂ OEt) ₂	2, 4-Me ₂ -Ph	
	282	NH-3-pentyl	2, 4-Me ₂ -Ph	
	283	NMePh	2, 4-Me ₂ -Ph	
	284	NPr ₂	2, 4-Me ₂ -Ph	
	285	NH-3-hexyl	2, 4-Me ₂ -Ph	
15	286	morpholino	2, 4-Me ₂ -Ph	
	287	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2, 4-Me ₂ -Ph	
	288	NHCH(CH ₂ Ph)CH ₂ OMe	2, 4-Me ₂ -Ph	
	289	NH-4-tetrahydropyranyl	2, 4-Me ₂ -Ph	
	290	NH-cyclopentyl	2, 4-Me ₂ -Ph	
20	291	1, 2, 3, 4-tetrahydro-	2, 4-Me ₂ -Ph	
		isoquinolinyl		
	292	CH ₂ -(1, 2, 3, 4-tetrahydro-	2, 4-Me ₂ -Ph	
		isoquinolinyl)		
	293	OEt	2, 4-Me ₂ -Ph	
25	294	OCH(Et)CH ₂ OMe	2, 4-Me ₂ -Ph	
	295	OCH ₂ Ph	2, 4-Me ₂ -Ph	
	296	O-3-pentyl	2, 4-Me ₂ -Ph	
	297	SEt	2, 4-Me ₂ -Ph	
	298	S(O)Et	2, 4-Me ₂ -Ph	
30	299	SO ₂ Et	2, 4-Me ₂ -Ph	
	300	CH(CO ₂ Et) ₂	2, 4-Me ₂ -Ph	
	301	C(Et)(CO ₂ Et) ₂	2, 4-Me ₂ -Ph	
	302	CH(Et)CH ₂ OH	2, 4-Me ₂ -Ph	
	303	CH(Et)CH ₂ OMe	2, 4-Me ₂ -Ph	
35	304	CONMe ₂	2, 4-Me ₂ -Ph	
	305	COCH ₃	2, 4-Me ₂ -Ph	

			CH(OH)CH ₃	2,4-Me ₂ -Ph
			C(OH)Ph-3-pyridyl	2,4-Me ₂ -Ph
			Ph	2,4-Me ₂ -Ph
			2-CF ₃ -Ph	2,4-Me ₂ -Ph
5	306	N		
	307	N		
	308	N		
	309	N		
	310	N	2-Ph-Ph	2,4-Me ₂ -Ph
	311	N	3-pentyl	2,4-Me ₂ -Ph
	312	N	cyclobutyl	2,4-Me ₂ -Ph
10	313	N	3-pyridyl	2,4-Me ₂ -Ph
	314	N	CH(Et)CH ₂ CONMe ₂	2,4-Me ₂ -Ph
	315	N	CH(Et)CH ₂ CH ₂ NMe ₂	2,4-Me ₂ -Ph
	316 ^{an}	C-Me	NET ₂	2-Br-4-MeO-Ph
	317 ^{am}	C-Me	NH-3-pentyl	2-Br-4-MeO-Ph
	318 ^{aj}	C-Me	NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2,4,6-Me ₃ -Ph
	319 ^{ao}	C-Me	NH(c-C ₃ H ₅)	2,4-Me ₂ -Ph
15	320 ^{ak}	C-Me	morpholino	2,4,6-Me ₃ -Ph
	321 ^{ap}	C-Me	NHCH(CH ₂ OMe) ₂	2-CN-4-Me-Ph
	322 ^{aq}	C-Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4,6-Me ₃ -Ph
	324 ^{as}	C-Me	NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Me-4-Br-Ph
	325 ^{at}	C-Me	NHCH(CH ₂ OMe) ₂	2,5-Me ₂ -4-MeO-Ph
	326 ^{au}	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,5-Me ₂ -4-MeO-Ph
	327 ^{av}	C-Me	NH-3-pentyl	2,5-Me ₂ -4-MeO-Ph
20	328 ^{aw}	C-Me	NET ₂	2,5-Me ₂ -4-MeO-Ph
	329 ^{ax}	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MePh
	330 ^{ay}	C-Me	NCH(Et)CH ₂ OMe	2-Cl-4-MePh
	331 ^{az}	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MePh
	332 ^{ba}	C-Me	(S)-NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Cl-4-MePh
	333 ^{bb}	C-Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,5-Me ₂ -4-MeOPh
	334 ^{bg}	C-Me	NET ₂	2-Me-4-MeOPh
25	335 ^{bh}	C-Me	OEt	2-Me-4-MeOPh
	336 ^{bi}	C-Me	(S)-NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Me-4-MeOPh
	337 ^{bj}	C-Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2-Me-4-MeOPh
	338 ^{bk}	C-Me	NHCH(CH ₂ CH ₂ OEt) ₂	2-Me-4-MeOPh
	339	C-Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4-Cl ₂ -Ph
	340	C-Me	(S)-NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2,4-Cl ₂ -Ph
	341	C-Me	NH-3-pentyl	2-Me-4-BrPh
35	342	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-BrPh
				oil

343	C-Me	NHCH(CH ₂ -iPr)CH ₂ OMe	2, 4-Me ₂ -Ph	oil	
344	C-Me	NHCH(Pr)CH ₂ OMe	2, 4-Me ₂ -Ph	94-95	
345	C-Me	NHCH(Et)CH ₂ OEt	2, 4-Me ₂ -Ph	76-77	
346	C-Me	NHCH(CH ₂ OMe)CH ₂ CH ₂ OMe	2-Me-4-Me ₂ NPh	oil	
5	347	C-Me	NET ₂	2-Me-4-ClPh	oil
	348	C-Me	NH-3-pentyl	2-Me-4-ClPh	122-124
	349	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-ClPh	oil
	350	C-Me	NHCH(CH ₂ OMe) ₂	2-Me-4-ClPh	122-123
	351	C-Me	NET ₂	2-Me-4-ClPh	oil
10	352	C-Me	NET ₂	2-Cl-4-MePh	oil
	353	C-Me	NH-3-pentyl	2-Cl-4-MePh	120-121
	354	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MeOPh	
	355 ^{bl}	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MeOPh	oil
	356 ^{bm}	C-Me	NHCH(Et)CH ₂ OMe	2-Cl-4-MeOPh	108-110
15	357 ^{bn}	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4-MeOPh	127-129
	358 ^{bo}	C-Me	NET ₂	2-Cl-4-MeOPh	oil
	359 ^{bp}	C-Me	NH-3-pentyl	2-Cl-4-MeOPh	77-79
	360	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh	
	361	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh	
20	362	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4-MeOPh	
	363	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4-MeOPh	
	364	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh	
	365	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh	
	366	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl-4, 5-(MeO)2Ph	
25	367	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4, 5-(MeO)2Ph	
	368	C-Me	NHCH(Et)CH ₂ OMe	2-Cl-4, 5-(MeO)2Ph	
	369	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4, 5-(MeO)2Ph	
	370	C-Me	NET ₂	2-Cl-4, 5-(MeO)2Ph	
	371	C-Me	NH-3-pentyl	2-Cl-4, 5-(MeO)2Ph	
30	372	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4, 5-(MeO)2Ph	
	373	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4, 5-(MeO)2Ph	
	374 ^{bq}	C-Me	NHCH(CH ₂ OMe) ₂	2-Br-4, 5-(MeO)2Ph	137-138
	375	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4, 5-(MeO)2Ph	
	376 ^{br}	C-Me	NHCH(Et)CH ₂ OMe	2-Br-4, 5-(MeO)2Ph	147-148
35	377	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4, 5-(MeO)2Ph	
	378 ^{bs}	C-Me	NET ₂	2-Br-4, 5-(MeO)2Ph	52-58

	379	C-Me	NH-3-pentyl	2-Br-4,5-(MeO)2Ph
	380	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4,5-(MeO)2Ph
	381	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4,5-(MeO)2Ph
	382	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl-4,6-(MeO)2Ph
5	383	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,6-(MeO)2Ph
	384	C-Me	NHCH(Et)CH ₂ OMe	2-Cl-4,6-(MeO)2Ph
	385	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4,6-(MeO)2Ph
	386	C-Me	NET ₂	2-Cl-4,6-(MeO)2Ph
	387	C-Me	NH-3-pentyl	2-Cl-4,6-(MeO)2Ph
	10	388	C-Me	NHCH(Et)CH ₂ CH ₂ OMe
	389	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4,6-(MeO)2Ph
	390	C-Me	NHCH(CH ₂ OMe) ₂	2-Me-4,6-(MeO)2Ph
	391	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4,6-(MeO)2Ph
	392	C-Me	NHCH(Et)CH ₂ OMe	2-Me-4,6-(MeO)2Ph
15	393	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me-4,6-(MeO)2Ph
	395	C-Me	NET ₂	2-Me-4,6-(MeO)2Ph
	396	C-Me	NH-3-pentyl	2-Me-4,6-(MeO)2Ph
	397	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4,6-(MeO)2Ph
	398	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4,6-(MeO)2Ph
20	399	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4,6-(MeO)2Ph
	400	C-Me	NET ₂	2-Br-4,6-(MeO)2Ph
	401	C-Me	NH-3-pentyl	2-Br-4,6-(MeO)2Ph
	402	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4,6-(MeO)2Ph
	403	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4,6-(MeO)2Ph
25	404	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	405	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	406	C-Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-MePh
	407	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-MePh
	408	C-Me	NHCH(Et)CH ₂ OMe	2-Me0-4-MePh
30	409	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me0-4-MePh
	410	C-Me	NET ₂	2-Me0-4-MePh
	411	C-Me	NH-3-pentyl	2-Me0-4-MePh
	412	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me0-4-MePh
	413	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me0-4-MePh
35	414	C-Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-MePh
	415	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-MePh

	416	C-Me	NHCH(Et)CH ₂ OMe	2-MeO-4-MePh
	417	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-MePh
	418	C-Me	NET ₂	2-MeO-4-MePh
	419	C-Me	NH-3-pentyl	2-MeO-4-MePh
5	420	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-MePh
	421	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-MePh
	423bt	C-Me	NHCH(CH ₂ OMe) ₂	2-MeO-4-ClPh
	424	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-ClPh
	425	C-Me	NHCH(Et)CH ₂ OMe	2-MeO-4-ClPh
10	426	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-ClPh
	427	C-Me	NET ₂	2-MeO-4-ClPh
	428	C-Me	NH-3-pentyl	2-MeO-4-ClPh
	429	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-MeO-4-ClPh
	430	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-ClPh
15				
		NOTES FOR TABLE 1:		
	a)	Analysis Calcd: C, 52.69, H, 5.17, N, 17.07, Cl, 17.28; Found: C, 52.82, H, 5.06, N, 16.77, Cl, 17.50.		
20	b)	CI-HRMS: Calcd: 406.1565, Found: 405.1573 (M + H); Analysis Calcd: C: 59.11; H: 6.20; N: 17.23; Cl: 17.45; Found: C: 59.93; H: 6.34; N: 16.50; Cl: 16.95; NMR (CDCl ₃ , 300 MHz): 0.95 (t, J = 8, 4H), 1.30-1.40 (m, 4H), 1.50-1.75 (m, 4H), 2.35 (s, 3H), 2.48 (s, 3H), 4.30-4.45 (m, 1H), 6.15 (d, J = 8, 1H), 7.30 (s, 2H), 7.50 (s, 1H)		
25	c)	CI-HRMS: Calcd: 392.1409, Found: 392.1388 (M + H); NMR (CDCl ₃ , 300 MHz): 1.00 (t, J = 8, 3H), 1.35 (t, J = 8, 3H), 1.41 (q, J = 8, 2H), 1.65-1.85 (m, 2H), 2.30 (s, 3H), 2.40 (s, 3H), 3.85-4.20 (m, 4H), 7.30 (s, 2H), 7.50 (s, 1H).		
30	d)	CI-HRMS: Calcd: 404.1409, Found: 404.1408 (M + H); NMR (CDCl ₃ , 300 MHz): 0.35-0.45 (m, 2H), 0.52-0.62 (m, 2H), 0.98 (t, J = 8, 3H), 1.70-1.90 (m, 2H),		
35				

2.30 (s, 3H), 2.40 (s, 3H), 3.85-4.02 (m, 2H),
4.02-4.20 (m, 2H), 7.30 (s, 2H), 7.50 (s, 1H).

e) CI-HRMS: Calcd: 424.1307, Found: 424.1307 (M + H);
NMR (CDCl₃, 300 MHz): 2.28 (s, 3H), 2.40 (s, 3H),
3.40 (s, 6H), 3.75 (t, J = 8, 4H), 4.20-4.45 (m,
4H), 7.30 (s, 2H), 7.50 (s, 1H).

f) CI-HRMS: Calcd: 406.1565, Found: 406.1578 (M + H);
NMR (CDCl₃, 300 MHz): 0.90 (t, J = 8, 3H), 1.00 (t,
J = 8, 3H), 1.28-1.45 (m, 4H), 1.50-1.80 (m, 4H),
2.35 (s, 3H), 2.50 (s, 3H), 4.20-4.35 (m, 1H),
6.10-6.23 (m, 1H), 7.30 (s, 2H), 7.50 (s, 1H).

g) CI-HRMS: Calcd: 394.1201, Found: 394.1209 (M + H);
NMR (CDCl₃, 300 MHz): 1.02 (t, J = 8, 3H), 1.65-
1.90 (m, 2H), 2.35 (s, 3H), 2.48 (s, 3H), 3.40 (s,
3H), 3.50-3.60 (m, 2H), 4.35-4.45 (brs, 1H), 6.50-
6.60 (m, 1H), 7.30 (s, 2H), 7.50 (s, 1H).

h) CI-HRMS: Calcd: 364.1096, Found: 364.1093 (M + H);
Analysis: Calcd: C: 56.05; H: 5.27; N: 19.23; Cl:
19.46; Found: C: 55.96; H: 5.24; N: 18.93; Cl:
19.25;
NMR (CDCl₃, 300 MHz): 1.35 (t, J = 8, 6H), 2.30 (s,
3H), 2.40 (s, 3H), 3.95-4.15 (m, 4H), 7.30 (s, 2H),
7.50 (d, J = 1, 1H).

i) CI-HRMS: Calcd: 438.1464, Found: 438.1454 (M + H);
NMR (CDCl₃, 300 MHz): 1.22 (t, J = 8, 6H), 2.35 (s,
3H), 2.47 (s, 3H), 3.39 (q, J = 8, 4H), 3.65 (dd, J
= 8, 1, 2H), 3.73 (dd, J = 8, 1, 2H), 4.55-4.65 (m,
1H), 6.75 (d, J = 8, 1H), 7.30 (d, J = 1, 2H), 7.50
(s, 1H).

j) CI-HRMS: Calcd: 378.1252, Found: 378.1249 (M + H);
Analysis: Calcd: C: 57.15; H: 5.61; N: 18.51; Cl:
18.74; Found: C: 57.56; H: 5.65; N: 18.35; Cl:
18.45;
NMR (CDCl₃, 300 MHz): 1.00 (t, J = 8, 6H), 1.55-
1.70 (m, 2H), 1.70-1.85 (m, 2H), 2.35 (s, 3H), 2.50

- (s, 3H), 4.15-4.25 (m, 1H), 6.18 (d, $J = 8$, 1H),
 7.30 (s, 2H), 7.50 (s, 1H).
- 5 k) CI-HRMS: Calcd: 398.0939, Found: 398.0922 (M + H);
 Analysis: Calcd: C: 60.31; H: 4.30; N: 17.58; Cl:
 17.80; Found: C: 60.29; H: 4.59; N: 17.09; Cl:
 17.57;
 NMR (CDCl₃, 300 MHz): 2.05 (s, 3H), 2.50 (s, 3H),
 3.78 (s, 3H), 7.20-7.45 (m, 7H), 7.50 (d, $J = 1$,
 1H).
- 10 l) CI-HRMS: Calcd: 392.1409, Found: 392.1391 (M + H);
 NMR (CDCl₃, 300 MHz): 0.98 (t, $J = 8$, 6H), 1.70-
 1.85 (m, 4H), 2.30 (s, 3H), 2.40 (s, 3H), 3.80-4.10
 (m, 4H), 7.30 (s, 2H), 7.50 (d, $J = 1$, 1H).
- 15 m) CI-HRMS: Calcd: 392.1409, Found: 392.1415 (M + H);
 Analysis: Calcd: C: 58.17; H: 5.92; N: 17.85; Cl:
 18.07; Found: C: 58.41; H: 5.85; N: 18.10; Cl:
 17.75;
 NMR (CDCl₃, 300 MHz): 0.90-1.05 (m, 6H), 1.35-1.55
 (m, 2H), 1.55-1.85 (m, 4H), 2.35 (s, 3H), 2.48 (s,
 3H), 4.20-4.35 (m, 1H), 6.15 (d, $J = 8$, 1H), 7.30
 (s, 2H), 7.50 (d, $J = 1$, 1H).
- 20 n) CI-HRMS: Calcd: 337.0623, Found: 337.0689 (M + H);
 Analysis: Calcd: C: 53.43; H: 4.18; N: 16.62; Cl:
 21.03, Found: C: 53.56; H: 4.33; N: 16.56; Cl:
 20.75;
 NMR (CDCl₃, 300 MHz): 1.60 (t, $J = 8$, 3H), 2.40 (s,
 3H), 2.55 (s, 3H), 4.80 (q, $J = 8$, 2H), 7.30 (d, J
 = 8, 1H), 7.35 (dd, $J = 8$, 1, 1H), 7.55 (d, $J = 1$,
 1H)
- 25 o) CI-HRMS: Calcd: 383.2321, Found: 383.2309 (M + H);
 NMR (CDCl₃, 300 MHz): 2.00 (s, 6H), 2.20 (s, 3H),
 2.30 (s, 3H), 2.45 (s, 3H), 3.45 (s, 6H), 3.61 (dd,
 $J = 8$, 8, 2H), 3.70 (dd, $J = 8$, 8, 2H), 4.60-4.70
 (m, 1H), 6.70 (d, $J = 8$, 1H), 6.94 (s, 2H).
- 30 p) CI-HRMS: Calcd: 370.2243, Found: 370.2246 (M + H);
- 35

Analysis: Calcd: C: 65.02; H: 7.38; N: 18.96;
 Found: C: 65.22; H: 7.39; N: 18.71;
 NMR (CDCl_3 , 300 MHz): 2.18 (s, 3H), 2.30 (s, 3H),
 2.45 (s, 3H), 3.45 (s, 6H), 3.60 (dd, $J = 8, 8$,
 2H), 3.69 (dd, $J = 8, 8, 2\text{H}$), 4.60-4.70 (m, 1H),
 6.70 (d, $J = 8, 1\text{H}$), 7.05 (d, $J = 8, 1\text{H}$), 7.07 (c
 $J = 8, 1\text{H}$), 7.10 (s, 1H).

q) CI-HRMS: Calcd: 384.2400, Found: 384.2393 ($M + H$);
 NMR (CDCl_3 , 300 MHz): 2.16 (s, 3H), 2.25 (s, 3H),
 10 2.35 (s, 3H), 2.39 (s, 3H), 3.40 (s, 6H), 3.77 (t,
 $J = 8$, 4H), 4.20-4.45 (m, 4H), 7.02 (d, $J = 8$, 1H)
 7.05 (s, 1H), 7.10 (d, $J = 7$, 1H).

r) CI-HRMS: Calcd: 354.2294, Found: 354.2271 (M + H);
 Analysis: Calcd: C: 67.96; H: 7.71; N: 19.81;
 15 Found: C: 67.56; H: 7.37; N: 19.60;
 NMR (CDCl_3 , 300 MHz): 1.03 (t, $J = 8$, 3H), 1.65-
 1.88 (m, 2H), 2.17 (s, 3H), 2.30 (s, 3H), 2.35 (s,
 3H), 2.45 (s, 3H), 3.40 (s, 3H), 3.50-3.62 (m, 2H),
 4.30-4.45 (m, 1H), 6.51 (d, $J = 8$, 1H), 7.04 (d, J
 20 = 8, 1H), 7.10 (d, $J = 8$, 1H), 7.12 (s, 1H).

s) CI-HRMS: Calcd: 338.2345, Found: 338.2332 (M + H);
Analysis: Calcd: C: 71.18; H: 8.06; N: 20.75;
Found: C: 71.43; H: 7.80; N: 20.70;
NMR (CDCl_3 , 300 MHz): 1.00 (t, $J = 8$, 6H), 1.55-
1.70 (m, 2H), 1.70-1.85 (m, 2H), 2.19 (s, 3H), 2.30
(s, 3H), 2.35 (s, 3H), 2.46 (s, 3H), 4.15-4.26 (m,
1H), 6.17 (d, $J = 8$, 1H), 7.06 (d, $J = 8$, 1H), 7.10
(d, $J = 1$, 1H), 7.13 (s, 1H).

t) CI-HRMS: Calcd: 324.2188, Found: 324.2188 ($M + H$);
 30 NMR (CDCl_3 , 300 MHz): 1.25 (t, $J = 8$, 6H), 2.16 (s,
 3H), 2.28 (s, 3H), 2.35 (s, 3H), 2.40 (s, 3H),
 3.95-4.20 (m, 4H), 7.05 (dd, $J = 8, 1$, 1H), 7.07
 (s, 1H), 7.10 (d, $J = 1$, 1H)

u) CI-^{HR}MS: Calcd: 346.1780, Found: 346.1785 (M + H);
35 Analysis: Calcd: C: 66.07; H: 5.54; N: 28.39;
Found: C: 66.07; H: 5.60; N: 27.81;

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- NMR (CDCl₃, 300 MHz): 2.15 (s, 3H), 2.32 (s, 3H)
 2.17 (s, 3H), 2.52 (s, 3H), 5.25-5.35 (m, 4H), 7.08
 (s, 2H), 7.15 (s, 1H).
- v) CI-HRMS: Calcd: 340.2137, Found: 340.2137 (M + H);
 Analysis: Calcd: C: 67.23; H: 7.42; N: 20.63;
 Found: C: 67.11; H: 7.39; N: 20.26;
 NMR (CDCl₃, 300 MHz): 1.40 (d, J = 8, 3H), 2.16 (s,
 3H), 2.32 (s, 3H), 2.35 (s, 3H), 2.47 (s, 3H), 3.42
 (s, 3H), 3.50-3.60 (m, 2H), 4.50-4.15 (m, 1H), 6.56
 (d, J = 8, 1H), 7.00-7.15 (m, 3H).
- w) CI-HRMS: Calcd: 355.2134, Found: 355.2134 (M + H);
 NMR (CDCl₃, 300 MHz): 1.05 (t, J = 8, 3H), 1.85-
 2.00 (m, 2H), 2.17 (s, 3H), 2.36 (s, 6H), 2.50 (s,
 3H), 3.41 (s, 3H), 3.45 (dd, J = 8, 3, 1H), 3.82
 (dd, J = 8, 1, 1H), 5.70-5.80 (m, 1H), 7.00-7.20
 (m, 3H).
- x) CI-HRMS: Calcd: 364.2501, Found: 364.2501 (M + H);
 NMR (CDCl₃, 300 MHz): 0.35-0.43 (m, 2H), 0.50-0.60
 (m, 2H), 0.98 (t, J = 8, 3H), 1.20-1.30 (m, 1H),
 1.72-1.90 (m, 2H), 2.18 (s, 3H) 2.28 (s, 3H), 2.35
 (s, 3H), 2.40 (s, 3H), 3.88-4.03 (m, 2H), 4.03-4.20
 (m, 2H), 7.00-7.15 (m, 3H).
- y) CI-HRMS: Calcd: 353.2454, Found: 353.2454 (M + H);
 Analysis: Calcd: C: 68.15; H: 8.02; N: 23.84;
 Found: C: 67.43; H: 7.81; N: 23.45;
 NMR (CDCl₃, 300 MHz): 1.38 (d, J = 8, 3H), 2.18 (s,
 3H), 2.30-2.40 (m, 12H), 2.47 (s, 3H), 2.60-2.75
 (m, 2H), 4.30-4.50 (m, 1H), 6.60-6.70 (m, 1H),
 7.00-7.15 (m, 3H).
- z) CI-HRMS: Calcd: 361.2140, Found: 361.2128 (M + H);
 NMR (CDCl₃, 300 MHz): 0.75-0.83 (m, 2H), 1.00-1.10
 (m, 2H), 2.17 (s, 3H), 2.30 (s, 3H), 2.36 (s, 3H),
 2.47 (s, 3H), 2.85 (t, J = 8, 2H), 3.30-3.40 (m,
 1H), 4.40-4.55 (m, 2H), 7.00-7.18 (m, 3H).
- aa) CI-HRMS: Calcd: 363.2297, Found: 363.2311 (M + H);

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- NMR (CDCl₃, 300 MHz): 1.01 (t, 3H, J=8), 1.75-1.90
 (m, 2H), 2.15 (s, 3H), 2.19 (s, 3H), 2.35 (s, 3H),
 2.40 (s, 3H), 2.40 (s, 3H), 2.98 (t, 2H, J = 8),
 3.97-4.15 (m, 2H), 4.15-4.30 (m, 2H), 7.03 (d, 1H,
 1H), 7.08 (d, 1H, J = 8), 7.10 (s, 1H).
- 5 ab) CI-HRMS: Calcd: 363.2297, Found: 363.2295 (M + H);
 NMR (CDCl₃, 300 MHz): 1.01 (t, 3H, J = 8), 1.35-
 1.55 (m, 2H), 1.75-1.90 (m, 2H), 2.15 (s, 3H), 2.30
 (s, 3H), 2.36 (s, 3H), 2.46 (s, 3H), 4.10-4.30 (m,
 2H), 4.95-5.10 (br s, 2H), 7.05 (d, 1H, J = 8),
 7.10 (d, 1H, J = 8), 7.15 (s, 1H).
- 10 ac) CI-HRMS: Calcd: 368.2450, Found: 368.2436;
 Analysis: Calcd: C, 68.62, H, 7.95, N, 19.06;
 Found: C, 68.73, H, 7.97, N, 19.09; NMR (CDCl₃, 300
 MHz): 1.05 (t, J = 8, 3H), 1.70-1.90 (m, 2H), 2.01
 (d, J = 3, 6H), 2.20 (s, 3H), 2.30 (s, 3H), 2.46,
 2.465 (s, s, 3H), 3.42, 3.48 (s, s, 3H), 3.53-3.63
 (m, 2H), 4.35-4.45 (m, 1H), 6.73 (d, J = 8, 1H),
 6.97 (s, 2H).
- 15 ad) CI- HRMS: Calcd: 352.2501, Found: 352.2500 (M +
 H); Analysis: Calcd: C: 71.76; H: 8.33; N: 19.92,
 Found: C: 71.55; H: 8.15; N: 19.28;
 NMR (CDCl₃, 300 MHz): 1.01(t, J = 8, 6H), 1.58 -
 1.70 (m, 2H), 1.70-1.85 (m, 2H), 2.02 (s, 6H), 2.19
 (s, 3H), 2.45 (s, 3H), 4.12-4.28 (m, 1H), 6.18 (d,
 J = 8, 1H), 6.95 (s, 2H).
- 20 ae) CI- HRMS: Calcd: 398.2556, Found: 398.2551 (M +
 H); Analysis: Calcd: C: 66.47; H: 7.86; N: 17.62,
 Found: C: 66.74; H: 7.79; N: 17.70;
 NMR (CDCl₃, 300 MHz): 2.00 (s, 6H), 2.12 (s, 3H),
 2.30 (s, 3H), 2.37 (s, 3H), 3.40 (s, 6H), 3.78 (t,
 J = 8, 4H), 4.25-4.40 (m, 4H), 6.93 (s, 2H).
- 25 af) CI-HRMS: Calcd: 450.1141, Found: 450.1133 (M + H);

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Analysis: Calcd: C: 50.67; H: 5.37; N: 15.55; Br: 17.74; Found: C: 52.36; H: 5.84; N: 14.90; Br: 17.44;
 5 NMR (CDCl₃, 300 MHz): 2.32 (s, 3H), 2.57 (s, 3H), 3.42 (s, 6H), 3.60 (q, J = 8, 2H), 3.69 (q, J = 8, 2H), 3.82 (s, 3H), 4.60-4.70 (m, 1H), 6.73 (d, J = 8, 1H), 6.93 (dd, J = 8, 1, 1H), 7.22 (d, J = 8, 1H).
 10 ag) CI-HRMS: Calcd: 434.1192, Found: 434.1169 (M + H);
 Analysis: Calcd: C: 52.54; H: 5.58; N: 16.12; Br: 18.40; Found: C: 52.57; H: 5.60; N: 15.98; Br: 18.22;
 15 NMR (CDCl₃, 300 MHz): 1.00-1.07 (m, 3H), 1.65-1.85 (m, 2H), 2.35 (s, 3H), 2.46, 2.47 (s, s, 3H), 3.40, 3.45 (s, s, 3H), 3.83 (s, 3H), 4.35-4.45 (m, 1H), 6.55 (d, J = 8, 1H), 6.92 (dd, J = 8, 1, 1H), 7.20-7.30 (m, 2H).
 ah) CI-HRMS: Calcd: 337.2266, Found: 337.2251 (M + H);
 Analysis: Calcd: C: 70.18; H: 8.06; N: 20.75;
 20 Found: C: 70.69; H: 7.66; N: 20.34;
 NMR (CDCl₃, 300 MHz): 1.35 (t, J = 8, 6H), 2.01 (s, 6H), 2.15 (s, 3H), 2.30 (s, 3H), 2.38 (s, 3H), 4.07 (q, J = 8, 4H), 6.93 (s, 2H).
 ai) CI-HRMS: Calcd: 412.2713, Found: 412.2687 (M + H);
 25 Analysis: Calcd: C: 67.13; H: 8.08; N: 17.02;
 Found: C: 67.22; H: 7.85; N: 17.13;
 NMR (CDCl₃, 300 MHz): 1.24 (t, J = 8, 6H), 2.00 (s, 6H), 2.20 (s, 3H), 2.30 (s, 3H), 2.43 (s, 3H), 3.60 (q, J = 8, 4H), 3.66 (dd, J = 8, 3, 2H), 3.75 (dd, J = 8, 3, 2H), 4.55-4.65 (m, 1H), 6.75 (d, J = 8, 1H), 6.95 (s, 2H).
 30 aj) CI-HRMS: Calcd: 398.2556, Found: 398.2545 (M + H);
 Analysis: Calcd: C: 66.47; H: 7.86; N: 17.62;
 Found: C: 66.87; H: 7.62; N: 17.75;
 35 NMR (CDCl₃, 300 MHz): 1.95-2.10 (m, 8H), 2.20 (s, 3H), 2.32 (s, 3H), 2.44 (s, 3H), 3.38 (s, 3H), 3.42

- (s, 3H), 3.50-3.70 (m, 4H), 4.58-4.70 (m, 1H), 6.87
(d, J = 8, 1H), 6.95 (s, 2H).
- 5 ak) CI-HRMS: Calcd: 338.1981, Found: 338.1971 (M + H);
Analysis: Calcd: C: 67.63; H: 6.87; N: 20.06;
Found: C: 67.67; H: 6.82; N: 20.31;
NMR (CDCl₃, 300 MHz): 2.15 (s, 3H), 2.29 (s, 3H),
2.35 (s, 3H), 2.43 (s, 3H), 3.90 (t, J = 8, 4H),
4.35-4.45 (m, 4H), 7.00-7.15 (m, 3H).
- 10 al) CI-HRMS: Calcd: 464.1297, Found: 464.1297 (M + H);
NMR (CDCl₃, 300 MHz): 2.28 (s, 3H), 2.40 (s, 3H),
3.40 (s, 6H), 3.75 (t, J = 8, 4H), 3.83 (s, 3H),
4.20-4.50 (m, 4H), 6.93 (dd, J = 8, 1, 1H), 7.20
(s, 1H), 7.24 (d, J = 1, 1H).
- 15 am) CI-HRMS: Calcd: 418.1242, Found: 418.1223 (M + H);
NMR (CDCl₃, 300 MHz): 1.00 (t, d, J = 8, 1, 6H),
1.55-1.75 (m, 4H), 2.34 (s, 3H), 2.49 (s, 3H), 2.84
(s, 3H), 4.15-4.27 (m, 1H), 6.19 (d, J = 8, 1H),
6.93 (dd, J = 8, 1, 1H), 7.21-7.30 (m, 2H).
- 20 an) CI-HRMS: Calcd: 404.1086, Found: 404.1079 (M + H);
NMR (CDCl₃, 300 MHz): 1.35 (t, J = 8, 6H), 2.28 (s,
3H), 2.40 (s, 3H), 3.83 (s, 3H), 3.90-4.08 (m, 2H),
4.08-4.20 (m, 2H), 6.92 (dd, J = 8, 1, 1H), 7.20-
7.25 (m, 2H).
- 25 ao) CI-HRMS: Calcd: 308.1875, Found: 308.1872 (M + H);
NMR (CDCl₃, 300 MHz): 0.75-0.80 (m, 2H), 0.93-1.00
(m, 2H), 2.16 (s, 3H), 2.28 (s, 3H), 2.35 (s, 3H),
2.53 (s, 3H), 3.00-3.10 (m, 1H), 6.50-6.55 (m, 1H),
7.00-7.15 (m, 3H).
- 30 ap) CI-HRMS: Calcd: 397.1988, Found: 397.1984 (M + H);
NMR (CDCl₃, 300 MHz): 2.43 (s, 3H), 2.50 (s, 3H),
3.43 (s, 3H), 3.61 (dd, J = 8, 8, 2H), 3.69 (dd, J =
8, 8, 2H), 3.88 (s, 3H), 4.58-4.70 (m, 1H), 6.75
(d, J = 8, 1H), 7.20 (dd, J = 8, 1, 1H), 7.25 (d, J
= 1, 1H), 7.40 (s, 1H).
- 35 aq) CI-HRMS: Calcd: 375.2297, Found: 375.2286 (M + H);

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Analysis: Calcd: C: 70.56; H: 7.01; N: 22.44;
 Found: C: 70.49; H: 6.99; N: 22.45;
 NMR (CDCl₃, 300 MHz): 0.79-0.85 (m, 2H), 1.00-1.05
 (m, 1H), 2.00 (s, 6H), 2.19 (s, 3H), 2.32 (s, 3H),
 5 2.44 (s, 3H), 2.84 (t, J = 8, 2H), 3.30-3.40 (m,
 1H), 4.50 (t, J = 8, 2H), 6.95 (s, 2H).
 ar) CI-HRMS: Calcd: 434.1192, Found: 434.1189 (M + H);
 Analysis: Calcd: C: 52.54; H: 5.58; N: 16.12; Br:
 10 18.40; Found: C: 52.75; H: 5.59; N: 16.09; Br:
 18.67;
 NMR (CDCl₃, 300 MHz): 2.19 (s, 3H), 2.30 (s, 3H),
 2.47 (s, 3H), 3.43 (s, 6H), 3.60 (dd, J = 8, 8,
 2H), 3.70 (dd, J = 8, 8, 2H), 4.58-4.70 (m, 1H),
 15 6.71 (d, J = 8, 1H), 7.08 (d, J = 8, 1H), 7.37 (dd,
 J = 8, 1, 1H), 7.45 (d, J = 1, 1H).
 as) CI-HRMS: Calcd: 448.1348, Found: 448.1332 (M + H);
 Analysis: Calcd: C: 53.58; H: 5.85; N: 16.62; Br:
 17.82; Found: C: 53.68; H: 5.74; N: 15.52; Br:
 13.03;
 20 NMR (CDCl₃, 300 MHz): 1.95-2.10 (m, 2H), 2.20 (s,
 3H), 2.30 (s, 3H), 2.47 (s, 3H), 3.38 (s, 3H), 3.41
 (s, 3H), 3.50-3.67 (m, 4H), 4.55-4.70 (m, 1H), 6.89
 (d, J = 8, 1H), 7.05 (d, J = 8, 1H), 7.35 (dd, J =
 8, 1, 1H), 7.47 (d, J = 1, 1H).
 at) CI-HRMS: Calcd: 400.2349, Found: 400.2348 (M + H);
 Analysis: Calcd: C: 63.14; H: 7.32; N: 17.53;
 Found: C: 63.40; H: 7.08; N: 17.14;
 NMR (CDCl₃, 300 MHz): 2.16 (s, 3H), 2.20 (s, 3H),
 2.30 (s, 3H), 2.46 (s, 3H), 3.42 (s, 6H), 3.60 (q,
 30 J = 8, 2H), 3.70 (q, J = 8, 2H), 3.85 (s, 3H),
 4.59-4.70 (m, 1H), 6.70 (d, J = 8, 1H), 6.76 (s,
 1H), 6.96 (s, 1H).
 au) CI-HRMS: Calcd: 414.2505, Found: 414.2493 (M + H);
 NMR (CDCl₃, 300 MHz): 2.15 (s, 3H), 2.19 (s, 3H),
 35 2.25 (s, 3H), 2.40 (s, 3H), 3.40 (s, 6H), 3.76 (t,

J = 8, 4H), 3.84 (s, 3H), 4.20-4.45 (m, 4H), 6.77 (s, 1H), 6.93 (s, 1H).

av) CI-HRMS: Calcd: 368.2450, Found: 368.2447 (M + H); NMR (CDCl₃, 300 MHz): 1.00 (t, J = 8, 6H), 1.55-1.85 (m, 4H), 2.19 (s, 3H), 2.20 (s, 3H), 2.30 (s, 3H), 2.47 (s, 3H), 3.88 (s, 3H), 4.10-4.30 (m, 1H), 6.15 (d, J = 8, 1H), 6.78 (s, 1H), 6.98 (s, 1H).

aw) CI-HRMS: Calcd: 353.2216, Found: 353.2197 (M + H); NMR (CDCl₃, 300 MHz): 1.35 (t, J = 8, 6H), 2.17 (s, 3H), 2.19 (s, 3H), 2.28 (s, 3H), 2.40 (s, 3H), 3.85 (s, 3H), 3.90-4.20 (m, 4H), 6.78 (s, 1H), 6.95 (s, 1H).

ax) CI-HRMS: Calcd: 390.1697, Found: 390.1688 (M + H); Analysis: Calcd: C: 58.53; H: 6.20; N: 17.96; Cl: 9.09; Found: C: 58.95; H: 6.28; N: 17.73; Cl: 9.15; NMR (CDCl₃, 300 MHz): 2.35 (s, 3H), 2.37 (s, 3H), 2.48 (s, 3H), 3.42 (s, 6H), 3.60 (dd, J = 8, 8, 2H), 3.68 (dd, J = 8, 8, 2H), 4.59-4.72 (m, 1H), 6.72 (d, J = 8, 1H), 7.12 (d, J = 8, 1H), 7.23 (d, J = 8, 1H), 7.32 (s, 1H).

ay) CI-HRMS: Calcd: 374.1748, Found: 374.1735 (M + H); Analysis: Calcd: C: 61.04; H: 6.47; N: 18.73; Cl: 9.48; Found: C: 61.47; H: 6.54; N: 18.23; Cl: 9.61; NMR (CDCl₃, 300 MHz): 1.01 (t, J = 8, 3H), 1.62-1.88 (m, 4H), 2.35 (s, 3H), 2.37 (s, 3H), 2.48 (d, J = 1, 3H), 3.40, 3.45 (s, s, 3H), 3.50-3.64 (m, 2H), 4.38-4.47 (m, 1H), 6.53 (d, J = 8, 1H), 7.12 (d, J = 8, 1H), 7.07 (d, J = 8, 1H), 7.12 (s, 1H).

az) CI-HRMS: Calcd: 404.1853, Found: 404.1839 (M + H); NMR (CDCl₃, 300 MHz): 2.29 (s, 3H), 2.38 (s, 3H), 2.40 (s, 3H), 3.40 (s, 6H), 3.76 (t, J = 8, 4H), 4.20-4.45 (m, 4H), 7.11 (d, J = 8, 1H), 7.22 (d, J = 8, 1H), 7.31 (s, 1H).

ba) CI-HRMS: Calcd: 404.1853, Found: 404.1859 (M + H); Analysis: C: 59.47; H: 6.50; N: 17.34; Cl: 8.79; Found: C: 59.73; H: 6.46; N: 17.10; Cl: 8.73;

¹H NMR (CDCl₃, 300 MHz): 1.95-2.08 (m, 2H), 2.35 (s, 3H), 2.38 (s, 3H), 2.46 (s, 3H), 3.38 (s, 3H), 3.41 (s, 3H), 3.50-3.65 (m, 4H), 4.56-4.70 (m, 1H), 6.85 (d, J = 8, 1H), 7.12 (d, J = 8, 1H), 7.45 (d, J =

- 5 8, 1H), 7.32 (s, 1H).

bb) CI-HRMS: Calcd: 391.2246, Found: 391.2258 (M + H);
 Analysis: C: 67.67; H: 6.71; N: 21.52; Found: C:
 67.93; H: 6.70; N: 21.48;
 NMR (CDCl₃, 300 MHz): 0.76-0.84 (m, 2H), 0.84-0.91
 (m, 2H), 1.00-1.08 (m, 2H), 2.15 (s, 3H), 2.20 (s,
 3H), 2.29 (s, 3H), 2.45 (s, 3H), 2.85 (t, J = 8,
 2H), 3.28-3.30 (m, 1H), 3.85 (s, 3H), 6.78 (s, 1H),
 6.95 (s, 1H).

bc) CI-HRMS: Calcd: 386.2192, Found: 386.2181 (M + H);
 Analysis: C: 62.32; H: 7.06; N: 18.17; Found: C:
 62.48; H: 6.83; N: 18.15;
 NMR (CDCl₃, 300 MHz): 7.1 (d, 1H, J = 8), 6.9 (d,
 1H, J = 1), 6.8 (dd, 1H, J = 8,1), 6.7 (br.d, 1H,
 J = 8), 4.7-4.6 (m, 1H), 3.85 (s, 3H), 3.70-3.55
 (m, 4H), 3.45 (s, 6H), 2.5 (s, 3H), 2.3 (s, 3H),
 2.15 (s, 3H).

bd) CI-HRMS: Calcd: 400.2349, Found: 400.2336 (M + H);
 NMR (CDCl₃, 300 MHz): 7.1 (d, 1H, J = 7), 6.85 (d,
 1H, J = 1), 6.75 (dd, 1H, J = 7,1), 4.45-4.25
 (br.s, 4H), 3.75 (t, 4H, J = 7), 3.4 (s, 6H), 2.4
 (s, 3H), 2.25 (s, 3H), 2.15 (s, 3H).

be) CI-HRMS: Calcd: 370.2243, Found: 370.2247 (M + H);
 Analysis: C: 65.02; H: 7.38; N: 18.96; Found: C:
 65.28; H: 7.27; N: 18.71;
 NMR (CDCl₃, 300 MHz): 7.1 (d, 1H, J = 8), 6.85 (d,
 1H, J = 1), 6.8 (dd, 1H, J = 8,1), 6.5 (br. d, 1H,
 J = 1), 4.5-4.3 (m, 1H), 3.85 (s, 3H), 3.65-3.5 (m,
 2H), 3.4 (s, 2H), 2.5 (s, 3H), 2.3 (s, 3H), 2.2 (s,
 3H), 1.9-1.7 (m, 2H), 1.05 (t, 3H, J = 7).

bf) CI-HRMS: Calcd: 379.2246, Found: 379.2248 (M + H);

¹H NMR (CDCl₃, 300 MHz): 7.1 (d, 1H, J = 8), 6.85 (d, 1H, J = 1), 6.8 (dd, 1H, J = 8, 1), 4.3-4.0 (m, 4H), 3.85 (s, 3H), 3.0 (t, 2H, J = 7), 2.45 (s, 3H), 2.3 (s, 3H), 2.2 (s, 3H), 1.9-1.8 (m, 2H), 1.0 (t, 3H,

- | | |
|-----|--|
| | J = 7). |
| 5 | bg) CI-HRMS: Calcd: 340.2137, Found: 340.2122 (M + H);
NMR (CDCl ₃ , 300 MHz): 7.1 (d, 1H, J = 8), 6.85 (d,
1H, J = 1), 6.75 (dd, 1H, J = 8,1), 4.2-4.0 (br.m,
4H), 3.85 (s, 3H, 2.4 (s, 3H), 2.3 (s, 3H), 2.2
(s, 3H), 1.35 (t, 6H, J = 7). |
| 10 | bh) CI-HRMS: Calcd: 313.1665, Found: 313.6664 (M + H). |
| bi) | CI-HRMS: Calcd: 400.2349, Found: 400.2346 (M + H);
NMR (CDCl ₃ , 300 MHz): 7.1 (d, 1H, J = 7), 6.9-6.75
(m, 3H), 4.7-4.55 (m, 1H), 3.8 (s, 3H), 3.7-3.5 (m,
4H), 3.45 (s, 3H), 3.35 (s, 3H), 2.5 (s, 3H), 2.3
(s, 3H), 2.2 (s, 3H), 2.1-1.95 (m, 2H). |
| 15 | bj) CI-HRMS: Calcd: 377.2090, Found: 377.2092 (M + H);
Analysis: C: 67.00; H: 6.44; N: 22.32; Found: C:
67.35; H: 6.44; N: 22.23;
NMR (CDCl ₃ , 300 MHz): 7.1 (d, 1H, J = 8), 6.9 (d,
1H, J = 1), 6.8 (dd, 1H, J = 8,1), 4.55-4.4 (m,
2H), 3.85 (s, 3H), 3.4-3.3 (m, 1H), 2.85 (t, 2H, J
= 7), 2.5 (s, 3H), 2.3 (s, 3H), 2.2 (s, 3H), 1.1-
1.0 (m, 2H), 0.85-0.75 (m, 2H). |
| 20 | bk) CI-HRMS: Calcd: 413.2427, Found: 413.2416 (M + H);
NMR (CDCl ₃ , 300Hz): 7.1 (d, 1H, J = 8), 6.85 (d,
1H, J = 1), 6.75 (dd, 1H, J = 8,1), 4.6 (m, 1H),
3.85 (s, 3H), 3.75-3.6(m, 4H), 3.6 (q, 4H, J = 7),
2.5 (s, 3H), 2.3 s, 3H), 2.2 (s, 3H), 1.25 (t, 6H,
J = 7). |
| 25 | b1) CI-HRMS: Calcd: 420.1802, Found: 420.1825 (M + H);
bm) CI-HRMS: Calcd: 390.1697, Found: 390.1707 (M + H);
bn) CI-HRMS: Calcd: 397.1465, Found: 397.1462 (M + H);
bo) CI-HRMS: Calcd: 360.1513, Found: 360.1514 (M + H);
bp) CI-HRMS: Calcd: 374.1748, Found: 374.1737 (M + H); |
| 30 | |
| 35 | |

bq) CI-HRMS: Calcd: 479.1155, Found: 479.1154 (M + H);
 br) CI-HRMS: Calcd: 463.1219, Found: 463.1211 (M + H);
 Analysis Calcd: C: 51.96, H: 5.23, N, 15.15, Br:
 17.28; Found: C: 52.29, H: 5.62, N: 14.79, Br:
 5 17.47
 bs) CI-HRMS: Calcd: 433.1113, Found: 433.1114 (M, ^{79}Br);
 bt) NH₃-CI MS: Calcd: 406, Found: 406 (M + H)+;
 NMR (CDCl₃, 300 MHz) : δ 7.28 (d, J=10Hz, 1H), 7.03
 (d, J=8Hz, 1H), 6.96 (s, 1H), 6.7 (d, J=9, 1H),
 10 4.63 (m, 1H), 3.79 (s, 3H), 3.6 (m, 4H), 3.42 (s,
 6H), 2.47 (s, 3H), 2.32 (s, 3H).

15

EXAMPLE 431

Preparation of 2,4,7-dimethyl-8-(4-methoxy-2-methylphenyl)[1,5-a]-pyrazolo-1,3,5-triazine
 (Formula 1, where R³ is CH₃, R₁ is CH₃, Z is C-CH₃, Ar is
 2,4-dimethylphenyl)

20

5-Acetamidino-4-(4-methoxy-2-methylphenyl)-3-methylpyrazole, acetic acid salt (602 mg, 2 mmol) was mixed with a saturated NaHCO₃ solution (10 mL). The aqueous mixture was extracted with EtOAc three times.

25

The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The residue was taken up in toluene (10 mL) and trimethyl orthoacetate (0.36 g, 3 mmol) was added to the suspension. The reaction mixture was heated to reflux temperature under a nitrogen atmosphere and stirred for 16 hours. After being cooled to ambient temperature, the reaction mixture was concentrated in vacuo to give an oily solid. Column chromatography (CHCl₃:MeOH::9:1) afforded, after removal of solvent in vacuo, a yellow viscous oil (R_f = 0.6, 210 mg, 37% yield): NMR (CDCl₃, 300 MHz): 7.15 (d, 1H, J = 8), 6.9 (d, 1H, J = 1), 6.85 (dd, 1H, J = 8,1),

35

3.85 (s, 3H), 2.95 (s, 3H), 2.65 (s, 3H), 2.4 (s, 3H),
 2.15 (s, 3H); CI-HRMS: Calcd: 283.1559, Found:
 283.1554 (M + H).

5

EXAMPLE 432

10 7-hydroxy-5-methyl-3-(2-chloro-
 4-methylphenyl)pyrazolo[1,5-a]pyrimidine
 (Formula 1 where A is CH, R1 is Me, R3 is OH,
 Z is C-Me, Ar is 2-chloro-4-methylphenyl)

15 5-Amino-4-(2-chloro-4-methylphenyl)-3-
 methylpyrazole (1.86 g, 8.4 mmol) was dissolved in
 glacial acetic acid (30 mL) with stirring. Ethyl
 acetoacetate (1.18 mL, 9.2 mmol) was then added dropwise
 to the resulting solution. The reaction mixture was
 then heated to reflux temperature and stirred for 16
 20 hours, then cooled to room temperature. Ether (100 mL)
 was added and the resulting precipitate was collected by
 filtration. Drying in vacuo afforded a white solid (1.0 g,
 42% yield): NMR (CDCl₃, 300Hz): 8.70 (br.s 1H),
 7.29 (s, 1H), 7.21-7.09 (m, 2H), 5.62 (s, 1H), 2.35
 25 (s, 6H), 2.29 (s, 3H); CI-MS: 288 (M+H).

EXAMPLE 433

30 7-chloro-5-methyl-3-(2-chloro-
 4-methylphenyl)pyrazolo[1,5-a]pyrimidine
 (Formula 1 where A is CH, R1 is Me, R3 is Cl,
 Z is C-Me, Ar is 2-chloro-4-methylphenyl)

35 A mixture of 7-hydroxy-5-methyl-3-(2-chloro-4-
 methylphenyl)-pyrazolo[1,5-a]pyrimidine (1.0 g, 3.5
 mmol), phosphorus oxychloride (2.7 g, 1.64 mL, 17.4

mmol), N,N-diethylaniline (0.63 g, 0.7 mL, 4.2 mmol) and toluene (20 mL) was stirred at reflux temperature for 3 hours, then it was cooled to ambient temperature. The volatiles were removed in vacuo. Flash chromatography 5 (EtOAc:hexane::1:2) on the residue gave 7-chloro-5-methyl-3-(2-chloro-4-methylphenyl)-pyrazolo[1,5-a]pyrimidine (900 mg, 84% yield) as a yellow oil: NMR (CDCl₃, 300Hz): 7.35 (s, 1H), 7.28-7.26 (m, 1H), 71.6 (d, 1H, J = 7), 6.80 (s, 1H), 2.55 (s, 3H), 2.45 (s, 3H), 10 2.40 (s, 3H); CI- MS: 306 (M+H).

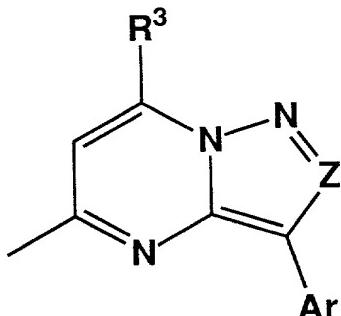
EXAMPLE 434

15 7-(pentyl-3-amino)-5-methyl-3-(2-chloro-4-methylphenyl)pyrazolo[1,5-a]pyrimidine
 (Formula 1 where A is CH, R1 is Me, R3 is pentyl-3-amino, Z is C-Me, Ar is 2-chloro-4-methylphenyl)

A solution of 3-pentylamine (394mg, 6.5 mmol) and 20 7-chloro-5-methyl-3-(2-chloro-4-methylphenyl)pyrazolo[1,5-a]pyrimidine (200 mg, 0.65 mmol) in dimethylsulfoxide (DMSO, 10 mL) was stirred at 150°C for 2 hours; then it was cooled to ambient temperature. The reaction mixture was then poured onto 25 water (100 mL) and mixed. Three extractions with dichloromethane, washing the combined organic layers with brine, drying over MgSO₄, filtration and removal of solvent in vacuo produced a yellow solid. Flash chromatography (EtOAc:hexanes::1:4) afforded a white 30 solid (140 mg, 60% yield): mp 139-141°C; NMR (CDCl₃, 300Hz): 7.32 (s, 1H), 7.27 (d, 1H, J = 8), 7.12 (d, 1H, J = 7), 6.02 (d, 1H, J = 9), 5.78 (s, 1H), 3.50-3.39 (m, 1H), 2.45 (s, 3H), 2.36 (s, 6H), 1.82-1.60 (m, 4H), 1.01 (t, 6H, J = 8); Analysis Calcd for C₂₀H₂₅ClN₄: C, 67.31, 35 H, 7.06, N, 15.70, Cl: 9.93; Found: C, 67.32, H, 6.95, N, 15.50, Cl, 9.93.

The examples delineated in TABLE 2 may be prepared by the methods outlined in Examples 1A, 1B, 432, 433, 434. Commonly used abbreviations are: Ph is phenyl, Pr is propyl, Me is methyl, Et is ethyl, Bu is butyl, Ex is Example, EtOAc is ethyl acetate.

TABLE 2



10

<u>Ex.</u>	<u>Z</u>	<u>R₃</u>	<u>Ar</u>	<u>mp (°C)</u>
435 ^b	C-Me	N(CH ₂ CH ₂ OMe) ₂	2, 4-Cl ₂ -Ph	71-73
436 ^c	C-Me	N(Bu)Et	2, 4-Cl ₂ -Ph	86-87
15 437 ^d	C-Me	NHCH(Et)CH ₂ OMe	2, 4-Cl ₂ -Ph	110-111
438 ^e	C-Me	N(Pr)CH ₂ CH ₂ CN	2, 4-Cl ₂ -Ph	83-85
439 ^f	C-Me	NH-3-pentyl	2, 4-Cl ₂ -Ph	175-176
440 ^g	C-Me	NHCH(CH ₂ OMe) ₂	2, 4-Cl ₂ -Ph	107
441 ^h	C-Me	NHCH(Et) ₂	2, 4-Me ₂ -Ph	oil
20 442 ⁱ	C-Me	NHCH(CH ₂ OMe) ₂	2, 4-Me ₂ -Ph	103-105
443 ^j	C-Me	N(CH ₂ CH ₂ OMe) ₂	2, 4-Me ₂ -Ph	87-89
444 ^k	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2, 4-Me ₂ -Ph	133 (dec)
445 ^l	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl, 4-MePh	77-78
446 ^m	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl, 4-MePh	131-133
25 447 ⁿ	C-Me	NHCH(Et) ₂	2-Cl, 4-MePh	139-141
448 ^o	C-Me	NET ₂	2, 4-Me ₂ -Ph	92-94
449 ^p	C-Me	N(Pr)CH ₂ CH ₂ CN	2, 4-Me ₂ -Ph	143-144
450 ^q	C-Me	N(Bu)CH ₂ CH ₂ CN	2, 4-Me ₂ -Ph	115-117
451 ^r	C-Me	NHCH(Et)CH ₂ OMe	2, 4-Me ₂ -Ph	oil

	452 ^s	C-Me	NHCH(Et) ₂	2-Me, 4-MeOPh	104-106
	453 ^t	C-Me	NHCH(CH ₂ OMe) ₂	2-Me, 4-MeOPh	115-116
	454 ^u	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me, 4-MeOPh	oil
	455 ^v	C-Me	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Me, 4-MeOPh	oil
5			(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2, 4-Me ₂ -Ph	oil
	456 ^w	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me, 4-ClPh	oil
	457 ^x	C-Me	NHET	2, 4-Me ₂ -Ph	oil
10	459 ^z	C-Me	NHCH(Et) ₂	2-Me, 4-ClPh	94-96
	460 ^{aa}	C-Me	NHCH(CH ₂ OMe) ₂	2-Me, 4-ClPh	113-114
	461 ^{ab}	C-Me	N(Ac)Et	2, 4-Me ₂ -Ph	oil
	462 ^{ac}	C-Me	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Me, 4-ClPh	oil
15	463 ^{ad}	C-Me	N(Pr)CH ₂ CH ₂ CN	2-Me, 4-MeOPh	118-119
	464 ^{ae}	C-Me	NET ₂	2-Me, 4-MeOPh	97-99
	465 ^{af}	C-Me	(S)-NHCH(CH ₂ CH ₂ OMe)- (CH ₂ OMe)	2-Cl, 4-MePh	101-103
	466 ^{ag}	C-Me	NET ₂	2-Cl, 4-MePh	129-130
20	467 ^{ah}	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me, 4-MeOPh	177-178
	468 ^{ai}	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl, 4-MePh	162-163
	469 ^{aj}	C-Me	NHCH(Et)CH ₂ OMe	2-Me, 4-MeOPh	oil
	470 ^{ak}	C-Me	NHCH(Et)CH ₂ OMe	2-Cl, 4-MePh	111-113
	471	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MeOPh	
25	472	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MeOPh	
	473	C-Me	NHCH(Et)CH ₂ OMe	2-Cl-4-MeOPh	
	474	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4-MeOPh	
	475	C-Me	NET ₂	2-Cl-4-MeOPh	
	476	C-Me	NH-3-pentyl	2-Cl-4-MeOPh	
30	477	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh	
	478	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh	
	479	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4-MeOPh	
	480	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4-MeOPh	
	481	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh	
35	482	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh	

			NHCH(CH ₂ OMe) ₂	2-Cl-4, 5-(MeO) 2Ph
	483	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4, 5-(MeO) 2Ph
	484	C-Me	NHCH(Et)CH ₂ OMe	2-Cl-4, 5-(MeO) 2Ph
	485	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4, 5-(MeO) 2Ph
	486	C-Me	NET ₂	2-Cl-4, 5-(MeO) 2Ph
5	487	C-Me	NH-3-pentyl	2-Cl-4, 5-(MeO) 2Ph
	488	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4, 5-(MeO) 2Ph
	489	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4, 5-(MeO) 2Ph
	490	C-Me	NHCH(CH ₂ OMe) ₂	2-Br-4, 5-(MeO) 2Ph
	491	C-Me	NET ₂	2-Br-4, 5-(MeO) 2Ph
10	492	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4, 5-(MeO) 2Ph
	493	C-Me	NHCH(Et)CH ₂ OMe	2-Br-4, 5-(MeO) 2Ph
	494	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4, 5-(MeO) 2Ph
	495	C-Me	NET ₂	2-Br-4, 5-(MeO) 2Ph
	496	C-Me	NH-3-pentyl	2-Br-4, 5-(MeO) 2Ph
15	497	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4, 5-(MeO) 2Ph
	498	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4, 5-(MeO) 2Ph
	499	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl-4, 6-(MeO) 2Ph
	500	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4, 6-(MeO) 2Ph
	501	C-Me	NHCH(Et)CH ₂ OMe	2-Cl-4, 6-(MeO) 2Ph
20	502	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4, 6-(MeO) 2Ph
	503	C-Me	NET ₂	2-Cl-4, 6-(MeO) 2Ph
	504	C-Me	NH-3-pentyl	2-Cl-4, 6-(MeO) 2Ph
	505	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4, 6-(MeO) 2Ph
	506	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4, 6-(MeO) 2Ph
25	507	C-Me	NHCH(CH ₂ OMe) ₂	2-Me-4, 6-(MeO) 2Ph
	508	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4, 6-(MeO) 2Ph
	509	C-Me	NHCH(Et)CH ₂ OMe	2-Me-4, 6-(MeO) 2Ph
	510	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me-4, 6-(MeO) 2Ph
	511	C-Me	NET ₂	2-Me-4, 6-(MeO) 2Ph
30	512	C-Me	NH-3-pentyl	2-Me-4, 6-(MeO) 2Ph
	513	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4, 6-(MeO) 2Ph
	514	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4, 6-(MeO) 2Ph
	515	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4, 6-(MeO) 2Ph
	516	C-Me	NET ₂	2-Br-4, 6-(MeO) 2Ph
35	517	C-Me	NH-3-pentyl	2-Br-4, 6-(MeO) 2Ph
	518	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4, 6-(MeO) 2Ph

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			2-Br-4, 6-(MeO)2Ph	
519	C-Me	NHCH(Me)CH ₂ CH ₂ OMe		
520	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh	
521	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh	
522	C-Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-MePh	
5	523	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-MePh
	524	C-Me	NHCH(Et)CH ₂ OMe	2-Me0-4-MePh
	525	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me0-4-MePh
	526	C-Me	NET ₂	2-Me0-4-MePh
	527	C-Me	NH-3-pentyl	2-Me0-4-MePh
10	528	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me0-4-MePh
	529	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me0-4-MePh
	530	C-Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-MePh
	531	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-MePh
	532	C-Me	NHCH(Et)CH ₂ OMe	2-Me0-4-MePh
15	533	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me0-4-MePh
	534	C-Me	NET ₂	2-Me0-4-MePh
	535	C-Me	NH-3-pentyl	2-Me0-4-MePh
	536	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me0-4-MePh
	537	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me0-4-MePh
20	538	C-Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-ClPh
	539	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-ClPh
	540	C-Me	NHCH(Et)CH ₂ OMe	2-Me0-4-ClPh
	541	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me0-4-ClPh
	542	C-Me	NET ₂	2-Me0-4-ClPh
25	543	C-Me	NH-3-pentyl	2-Me0-4-ClPh
	544	C-Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me0-4-ClPh
	545	C-Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me0-4-ClPh

NOTES FOR TABLE 2:

- 30 b) CI-HRMS: Calcd: 423.1355; Found: 423.1337 (M + H).
 c) Analysis: Calcd: C, 61.38, H, 6.18, N, 14.32;
 Found: C, 61.54, H, 6.12, N, 14.37.
 d) Analysis: Calcd: C: 58.02, H, 5.65, N, 14.24;
 35 Found: C, 58.11, H, 5.52, N, 14.26.

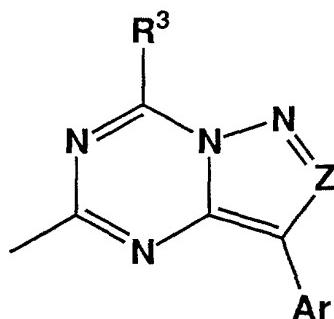
- PROCESSED BY SPIDER
- e) Analysis: Calcd: C, 59.71, H, 5.26, N, 14.85;
Found: C, 59.94, H, 5.09, N, 17.23.
- f) Analysis: Calcd: C, 60.48, H, 5.89, N, 14.85,
Found: C, 60.62, H, 5.88, N, 14.82.
- 5 h) CI-HRMS: Calcd: 337.2388; Found: 337.2392 (M + H).
- i) Analysis: Calcd: C, 68.45, H, 7.669, N, 15.21,
Found: C, 68.35, H, 7.49 N, 14.91.
- j) Analysis: Calcd: C, 69.08, H, 7.915, N, 14.65,
Found: C, 68.85, H, 7.83, N, 14.54.
- 10 k) Analysis: Calcd: C, 73.51, H, 7.01, N, 19.48,
Found: C, 71.57, H, 7.15, N, 19.12.
- l) CI-HRMS: Calcd: 403.1899; Found: 403.1901 (M + H).
- m) Analysis: Calcd: C, 61.77, H, 6.49, N, 14.41, Cl.
9.13; Found: C, 61.90, H, 6.66, N, 13.62, Cl, 9.25.
- 15 n) Analysis: Calcd: C, 67.31, H, 7.06, N, 15.70, Cl.
9.93; Found: C, 67.32, H, 6.95, N, 15.50, Cl, 9.93.
- o) Analysis: Calcd: C, 74.50, H, 8.14, N, 17.38,
Found: C, 74.43, H, 7.59, N, 17.16.
- p) Analysis: Calcd: C, 73.10, H, 7.54, N, 19.37,
Found: C, 73.18, H, 7.59, N, 18.81.
- 20 q) Analysis: Calcd: C, 73.57, H, 7.78, N, 18.65,
Found: C, 73.55, H, 7.79, N, 18.64.
- r) CI-HRMS: Calcd: 353.2333; Found: 353.2341 (M + H).
- s) Analysis: Calcd: C, 71.56, H, 8.02, N, 15.90,
Found: C, 71.45, H, 7.99, N, 15.88.
- 25 t) Analysis: Calcd: C, 65.60, H, 7.34, N, 14.57,
Found: C, 65.42, H, 7.24, N, 14.37.
- u) CI-HRMS: Calcd: 399.2398; Found: 399.2396 (M + H).
- v) CI-HRMS: Calcd: 399.2398; Found: 399.2396 (M + H).
- 30 w) CI-HRMS: Calcd: 383.2450; Found: 383.2447 (M + H).
- x) CI-HRMS: Calcd: 403.1887; Found: 403.1901 (M + H).
- y) CI-HRMS: Calcd: 295.1919; Found: 295.1923 (M + H).
- z) Analysis: Calcd: C, 67.31, H, 7.06, N, 15.70,
Found: C, 67.12, H, 6.86, N, 15.53.
- 35 aa) Analysis: Calcd: C, 61.77, H, 6.49, N, 14.41, Cl.
9.13; Found: C, 62.06, H, 6.37, N, 14.25, Cl, 9.12.

- ab) CI-HRMS: Calcd: 337.2017; Found: 337.2028 (M + H).
 ac) CI-HRMS: Calcd: 403.1893; Found: 403.1901 (M + H).
 ad) Analysis: Calcd: C, 70.00, H, 7.22, N, 18.55,
 Found: C, 70.05, H, 7.22, N, 18.36.
 5 ae) Analysis: Calcd: C, 70.98, H, 7.74, N, 16.55,
 Found: C, 71.15, H, 7.46, N, 16.56.
 ag) Analysis: Calcd: C, 66.59, H, 6.76, N, 16.34,
 Found: C, 66.69, H, 6.82, N, 16.20.
 ah) Analysis: Calcd: C, 70.38, H, 6.71, N, 18.65,
 10 Found: C, 70.35, H, 6.82, N, 18.83.
 ai) Analysis: Calcd: C, 66.39, H, 5.85, N, 18.44, Cl,
 9.33;
 Found: C, 66.29, H, 5.51, N, 18.36, Cl, 9.31.
 aj) CI-HRMS: Calcd: 369.2278; Found: 369.2291 (M + H).
 15 ak) Analysis: Calcd: C, 64.42, H, 6.77, N, 15.02,
 Found: C, 64.59, H, 6.51, N, 14.81.

The examples delineated in TABLE 3 may be prepared by
 20 the methods outlined in Examples 1, 2, 3 or 6. Commonly
 used abbreviations are: Ph is phenyl, Pr is propyl, Me
 is methyl, Et is ethyl, Bu is butyl, Ex is Example.

25

TABLE 3



<u>Ex.</u>	<u>Z</u>	<u>R₃</u>	<u>Ar</u>	<u>mp (°C)</u>
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	546 ^a	C-Me	NHCH(Et) ₂	2-Me-4-Me ₂ N-Ph	164-166
	547 ^b	C-Me	S-NHCH(CH ₂ CH ₂ OMe) -CH ₂ OMe	2,4-Me ₂ -Ph	oil
	548 ^c	C-Me	S-NHCH(CH ₂ CH ₂ OMe) -CH ₂ OMe	2-Me-4-Cl-Ph	oil
5					
	549 ^d	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me-4-Cl-Ph	115-116
	550 ^e	C-Me	NHCH(Et)CH ₂ CN	2-Me-4-Cl-Ph	131-132
	551 ^f	C-Me	N(Et) ₂	2,3-Me ₂ -4-OMe-Ph	oil
	552 ^g	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH ₂ OH	2,4-Cl ₂ -Ph	oil
10	553 ^h	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,3-Me ₂ -4-OMe-Ph	oil
	554 ⁱ	C-Me	NHCH(Et) ₂	2,3-Me ₂ -4-OMePh	123-124
	555 ^j	C-Me	N(CH ₂ -c-Pr)Pr	2-Me-4-Cl-Ph	oil
	556 ^k	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2,3-Me ₂ -4-OMePh	158-160
	557	C-Me	N(c-Pr)Et	2-Cl-4-OMePh	
15	558	C-Me	N(c-Pr)Me	2-Cl-4-OMePh	
	559	C-Me	N(c-Pr)Pr	2-Cl-4-OMePh	
	560	C-Me	N(c-Pr)Bu	2-Cl-4-OMePh	
	561 ^l	C-Me	N(Et) ₂	2-Cl-4-CN-Ph	115-117
	562	C-Me	N(c-Pr) ₂	2-Cl-4-OMe	127-129
20	563 ^m	C-Me	NHCH(CH ₂ OH) ₂	2,4-Cl ₂ -Ph	128-129
	564	C-Me	N(c-Pr)Et	2-Br-4,5-(MeO)2Ph	
	565	C-Me	N(c-Pr)Me	2-Br-4,5-(MeO)2Ph	
	566	C-Me	NH-c-Pr	2-Me-4-MeOPh	126-128
	567	C-Me	NHCH(Et)CH ₂ OH	2-Me-4-MeOPh	60-62
25	568	C-Me	NMe ₂	2-Br-4,5-(MeO)2Ph	
	569	C-Me	NHCH(Et) ₂	2-Me-4-MeOPh	103-105
	570	C-Me	N(c-Pr)Et	2-Me-4-MeOPh	173-174
	571	C-Me	NH-2-pentyl	2,4-Cl ₂ -Ph	118-120
	572	C-Me	NHCH(Et)CH ₂ CN	2,4-Cl ₂ -Ph	141-142
30	573	C-Me	NHCH(Pr)CH ₂ OMe	2,4-Cl ₂ -Ph	87-88
	574	C-Me	NHCH(CH ₂ -iPr)CH ₂ OMe	2,4-Cl ₂ -Ph	amorphous
	575	C-Me	NH-2-butyl	2,4-Me ₂ -Ph	oil
	576	C-Me	NH-2-pentyl	2,4-Me ₂ -Ph	oil
	577	C-Me	NH-2-hexyl	2,4-Me ₂ -Ph	oil
35	578	C-Me	NHCH(i-Pr)Me	2,4-Me ₂ -Ph	oil

579	C-Me	NHCH(Me)CH ₂ -iPr	2,4-Me ₂ -Ph	oil	
580	C-Me	NHCH(Me)-c-C ₆ H ₁₁	2,4-Me ₂ -Ph	oil	
581	C-Me	NH-2-indanyl	2,4-Me ₂ -Ph	oil	
582	C-Me	NH-1-indanyl	2,4-Me ₂ -Ph	oil	
5	583	C-Me	NHCH(Me)Ph	2,4-Me ₂ -Ph	oil
	584	C-Me	NHCH(Me)CH ₂ -(4-ClPh)	2,4-Me ₂ -Ph	oil
	585	C-Me	NHCH(Me)CH ₂ COCH ₃	2,4-Me ₂ -Ph	oil
	586	C-Me	NHCH(Ph)CH ₂ Ph	2,4-Me ₂ -Ph	oil
	587	C-Me	NHCH(Me)(CH ₂) ₃ NET ₂	2,4-Me ₂ -Ph	oil
10	588	C-Me	NH-(2-Ph-c-C ₃ H ₄)	2,4-Me ₂ -Ph	oil
	589	C-Me	NHCH(Et)CH ₂ CN	2,4-Me ₂ -Ph	119-120
	590	C-Me	NH-3-hexyl	2,4-Me ₂ -Ph	oil
	591 ⁿ	C-Me	NET ₂	2-MeO-4-ClPh	oil
	592 ^o	C-Me	NHCH(Et) ₂	2-MeO-4-ClPh	oil
15	593 ^p	C-Me	NHCH(Et)CH ₂ OMe	2-MeO-4-ClPh	oil
	594	C-Me	NMe ₂	2-MeO-4-ClPh	oil
	595 ^q	C-Me	NHCH(Et) ₂	2-OMe-4-MePh	oil
	596 ^r	C-Me	NET ₂	2-OMe-4-MePh	oil
	597 ^s	C-c-Pr	NHCH(CH ₂ OMe) ₂	2,4-Cl ₂ -Ph	oil
20	598	C-Me	N(c-Pr)Et	2,4-Me ₂ -Ph	
	599	C-Me	N(c-Pr)Et	2,4-Cl ₂ -Ph	
	600	C-Me	N(c-Pr)Et	2,4,6-Me ₃ -Ph	
	601	C-Me	N(c-Pr)Et	2-Me-4-Cl-Ph	
	602	C-Me	N(c-Pr)Et	2-Cl-4-Me-Ph	
25	603	C-Me	NHCH(c-Pr) ₂	2,4-Cl ₂ -Ph	
	604	C-Me	NHCH(c-Pr) ₂	2,4-Me ₂ -Ph	
	605	C-Me	NHCH(c-Pr) ₂	2-Me-4-Cl-Ph	
	606	C-Me	NHCH(c-Pr) ₂	2-Cl-4-Me-Ph	
	607	C-Me	NHCH(c-Pr) ₂	2-Me-4-OMe-Ph	
30	608	C-Me	NHCH(c-Pr) ₂	2-Cl-4-OMe-Ph	
	609	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl-5-F-OMePh	
	610	C-Me	NET ₂	2-Cl-5-F-OMePh	
	611	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-5-F-OMePh	
	612	C-Me	NHCH(Et) ₂	2-Cl-5-F-OMePh	
35	613	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-5-F-OMePh	
	614	C-Me	NET ₂	2,6-Me ₂ -pyrid-3-yl	

	615	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2,6-Me ₂ -pyrid-3-yl
	616	C-Me	NHCH(Et) ₂	2,6-Me ₂ -pyrid-3-yl
	617	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,6-Me ₂ -pyrid-3-yl
	618	C-OH	NHCH(CH ₂ OMe) ₂	2,4-Me ₂ -Ph
5	619	C-OH	NET ₂	2,4-Me ₂ -Ph
	620	C-OH	N(c-Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	621	C-OH	NHCH(Et) ₂	2,4-Me ₂ -Ph
	623	C-OH	N(CH ₂ CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	624	C-NET ₂	NHCH(CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	625	C-NET ₂	NET ₂	2,4-Me ₂ -Ph
10	626	C-NET ₂	N(c-Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	627	C-NET ₂	NHCH(Et) ₂	2,4-Me ₂ -Ph
	628	C-NET ₂	N(CH ₂ CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	629	C-Me	NHCH(Et) ₂	2-Me-4-CN-Ph
	15	630	C-Me	N(CH ₂ CH ₂ OMe) ₂

Notes for Table 3:

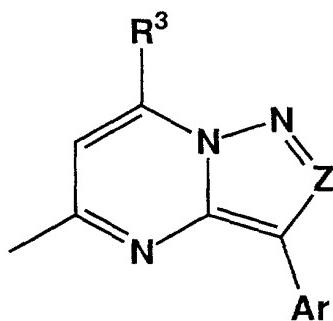
- a) CI-HRMS: Calcd: 367.2610, Found: 367.2607 (M + H);
- 20 b) CI-HRMS: Calcd: 384.2400, Found: 384.2393 (M + H);
- c) CI-HRMS: Calcd: 404.1853, Found: 404.1844 (M + H);
- d) CI-HRMS: Calcd: 381.1594, Found: 381.1596 (M + H);
Analysis: Calcd: C: 63.07, H, 5.57, N, 22.07, Cl,
9.32;
- 25 Found: C: 63.40, H, 5.55, N, 21.96, Cl: 9.15
- e) CI-HRMS: Calcd: 369.1594, Found: 369.1576 (M + H);
- f) CI-HRMS: Calcd: 354.2216, Found: 354.2211 (M + H);
- g) CI-HRMS: Calcd: 410.1072, Found: 410.1075 (M + H);
- h) CI-HRMS: Calcd: 414.2427, Found: 414.2427 (M + H);
- 30 i) CI-HRMS: Calcd: 368.2372, Found: 368.2372 (M + H);
- j) CI-HRMS: Calcd: 384.1955, Found: 384.1947 (M + H);
- k) CI-HRMS: Calcd: 391.2168, Found: 391.2160 (M + H);
- l) CI-HRMS: Calcd: 335.1984, Found: 335.1961 (M + H);
- m) CI-HRMS: Calcd: 382.0759, Found: 382.0765 (M + H);
- 35 n) NH₃-CI MS: Calcd: 360, Found: 360 (M + H)+
- o) NH₃-CI MS: Calcd: 374, Found: 374 (M + H)+;

- NMR (CDCl_3 , 300 MHz) : δ 7.29 (d, $J=8.4\text{Hz}$, 1H), 7.04 (dd, $J=1.8, 8\text{Hz}$, 1H), 6.96 (d, $J=1.8\text{Hz}$, 1H), 6.15 (d, $J=10$, 1H), 4.19 (m, 1H), 3.81 (s, 3H), 2.47 (s, 3H), 2.32 (s, 3H), 1.65 (m, 4H), 0.99 (t, $J=7.32\text{Hz}$, 6H)
- 5 p) $\text{NH}_3\text{-CI}$ MS: Calcd: 390, Found: 390 ($M + H$)⁺; NMR (CDCl_3 , 300 MHz) : δ 7.28 (d, $J=8\text{Hz}$, 1H), 7.03 (d, $J=8\text{Hz}$, 1H), 6.96 (s, 1H), 6.52 (d, $J=9\text{Hz}$, 1H), 4.36 (m, 1H), 3.8 (s, 3H), 3.55 (m, 2H), 3.39 (s, 3H), 2.47 (s, 3H), 2.32 (s, 3H), 1.76 (m, 2H), 1.01 (t, $J=7.32\text{Hz}$, 3H).
- 10 q) CI-HRMS: Calcd: 354.2294, Found: 354.2279 ($M + H$)⁺
- r) CI-HRMS: Calcd: 340.2137, Found: 340.2138 ($M + H$)⁺
- s) CI-HRMS: Calcd: 436.1307, Found: 436.1296 ($M + H$)⁺
- 15

The examples delineated in TABLE 4 may be prepared by the methods outlined in Examples 1A, 1B, 432, 433, 434. Commonly used abbreviations are: Ph is phenyl, Pr is propyl, Me is methyl, Et is ethyl, Bu is butyl, Ex is Example, EtOAc is ethyl acetate.

25

TABLE 4



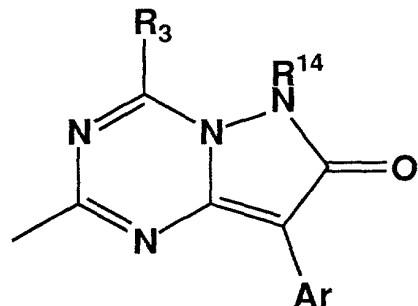
<u>Ex.</u>	<u>Z</u>	<u>R₃</u>	<u>Ar</u>	<u>mp (°C)</u>
	631	C-Me	NHCH(Et) ₂	2-Br-4,5-(MeO) ₂ Ph
	632	C-Me	NHCH(Et) ₂	2-Br-4-MeOPh
5	633	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-MeOPh
	634	C-Me	NHCH(CH ₂ OMe) ₂	2-Br-4-MeOPh
	635	C-Me	N(Et) ₂	2-Me-4-ClPh
	636	C-Me	N(c-Pr)Et	2,4-Cl ₂ Ph
	637	C-Me	N(c-Pr)Et	2,4-Me ₂ Ph
10	638	C-Me	N(c-Pr)Et	2,4,6-Me ₃ Ph
	639	C-Me	N(c-Pr)Et	2-Me-4-MeOPh
	640	C-Me	N(c-Pr)Et	2-Cl-4-MeOPh
	641	C-Me	N(c-Pr)Et	2-Cl-4-MePh
	642	C-Me	N(c-Pr)Et	2-Me-4-ClPh
15	643	C-Me	NHCH(c-Pr) ₂	2,4-Cl ₂ -Ph
	644	C-Me	NHCH(c-Pr) ₂	2,4-Me ₂ -Ph
	645	C-Me	NHCH(c-Pr) ₂	2-Me-4-Cl-Ph
	646	C-Me	NHCH(c-Pr) ₂	2-Cl-4-Me-Ph
	647	C-Me	NHCH(c-Pr) ₂	2-Me-4-OMe-Ph
20	648	C-Me	NHCH(c-Pr) ₂	2-Cl-4-OMe-Ph
	649	C-Me	NHCH(CH ₂ OMe) ₂	2-Cl-5-F-OMePh
	650	C-Me	NEt ₂	2-Cl-5-F-OMePh
	651	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-5-F-OMePh
	652	C-Me	NHCH(Et) ₂	2-Cl-5-F-OMePh
25	653	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-5-F-OMePh
	654	C-Me	NEt ₂	2,6-Me ₂ -pyrid-3-yl
	655	C-Me	N(c-Pr)CH ₂ CH ₂ CN	2,6-Me ₂ -pyrid-3-yl
	656	C-Me	NHCH(Et) ₂	2,6-Me ₂ -pyrid-3-yl
	657	C-Me	N(CH ₂ CH ₂ OMe) ₂	2,6-Me ₂ -pyrid-3-yl
30	658	C-OH	NHCH(CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	659	C-OH	NEt ₂	2,4-Me ₂ -Ph
	660	C-OH	N(c-Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	661	C-OH	NHCH(Et) ₂	2,4-Me ₂ -Ph
	662	C-OH	N(CH ₂ CH ₂ OMe) ₂	2,4-Me ₂ -Ph
35	663	C-NEt ₂	NHCH(CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	664	C-NEt ₂	NEt ₂	2,4-Me ₂ -Ph

665	C-NEt ₂	N(c-Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph	
666	C-NEt ₂	NHCH(Et) ₂	2,4-Me ₂ -Ph	
667	C-NEt ₂	N(CH ₂ CH ₂ OMe) ₂	2,4-Me ₂ -Ph	
668	C-Me	NHCH(Et) ₂	2-Me-4-CN-Ph	
5	669	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-CN-Ph

The examples in Tables 5 or 6 may be prepared by
10 the methods illustrated in Examples 1A, 1B, 2, 3, 6,
431, 432, 433, 434 or by appropriate combinations
thereof. Commonly used abbreviations are: Ph is phenyl,
Pr is propyl, Me is methyl, Et is ethyl, Bu is butyl, Ex
is Example.

15

Table 5



20

<u>Ex.</u>	<u>R₁₄</u>	<u>R₃</u>	<u>Ar</u>	
670	Me	NHCH(CH ₂ OMe) ₂	2,4-Cl ₂ -Ph	
671	Me	NHCHPr ₂	2,4-Cl ₂ -Ph	
25	672	Me	NETBu	2,4-Cl ₂ -Ph
673	Me	NPr(CH ₂ -c-C ₃ H ₅)	2,4-Cl ₂ -Ph	
674	Me	N(CH ₂ CH ₂ OMe) ₂	2,4-Cl ₂ -Ph	
675	Me	NH-3-heptyl	2,4-Cl ₂ -Ph	
676	Me	NHCH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph	

	677	Me	NET ₂	2,4-Cl ₂ -Ph
	678	Me	NHCH(CH ₂ OEt) ₂	2,4-Cl ₂ -Ph
	679	Me	NH-3-pentyl	2,4-Cl ₂ -Ph
	680	Me	NMePh	2,4-Cl ₂ -Ph
5	681	Me	NPr ₂	2,4-Cl ₂ -Ph
	682	Me	NH-3-hexyl	2,4-Cl ₂ -Ph
	683	Me	morpholino	2,4-Cl ₂ -Ph
	684	Me	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2,4-Cl ₂ -Ph
	685	Me	NHCH(CH ₂ Ph)CH ₂ OMe	2,4-Cl ₂ -Ph
	10	686	Me NH-4-tetrahydropyranyl	2,4-Cl ₂ -Ph
	687	Me	NH-cyclopentyl	2,4-Cl ₂ -Ph
	688	Me	OEt	2,4-Cl ₂ -Ph
	689	Me	OCH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph
	690	Me	OCH ₂ Ph	2,4-Cl ₂ -Ph
15	691	Me	O-3-pentyl	2,4-Cl ₂ -Ph
	692	Me	SEt	2,4-Cl ₂ -Ph
	693	Me	S(O)Et	2,4-Cl ₂ -Ph
	694	Me	SO ₂ Et	2,4-Cl ₂ -Ph
	695	Me	Ph	2,4-Cl ₂ -Ph
20	696	Me	2-CF ₃ -Ph	2,4-Cl ₂ -Ph
	697	Me	2-Ph-Ph	2,4-Cl ₂ -Ph
	698	Me	3-pentyl	2,4-Cl ₂ -Ph
	699	Me	cyclobutyl	2,4-Cl ₂ -Ph
	700	Me	3-pyridyl	2,4-Cl ₂ -Ph
25	701	Me	CH(Et)CH ₂ CONMe ₂	2,4-Cl ₂ -Ph
	702	Me	CH(Et)CH ₂ CH ₂ NMe ₂	2,4-Cl ₂ -Ph
	703	Me	NHCH(CH ₂ OMe) ₂	2,4,6-Me ₃ -Ph
	704	Me	NHCHPr ₂	2,4,6-Me ₃ -Ph
	705	Me	NETBu	2,4,6-Me ₃ -Ph
30	706	Me	NPr(CH ₂ -c-C ₃ H ₅)	2,4,6-Me ₃ -Ph
	707	Me	N(CH ₂ CH ₂ OMe) ₂	2,4,6-Me ₃ -Ph
	708	Me	NH-3-heptyl	2,4,6-Me ₃ -Ph
	709	Me	NHCH(Et)CH ₂ OMe	2,4,6-Me ₃ -Ph
	710	Me	NET ₂	2,4,6-Me ₃ -Ph
35	711	Me	NHCH(CH ₂ OEt) ₂	2,4,6-Me ₃ -Ph
	712	Me	NH-3-pentyl	2,4,6-Me ₃ -Ph

			NMePh	2, 4, 6-Me ₃ -Ph
			NPr ₂	2, 4, 6-Me ₃ -Ph
			NH-3-hexyl	2, 4, 6-Me ₃ -Ph
			morpholino	2, 4, 6-Me ₃ -Ph
5	717	Me	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2, 4, 6-Me ₃ -Ph
	718	Me	NHCH(CH ₂ Ph)CH ₂ OMe	2, 4, 6-Me ₃ -Ph
	719	Me	NH-4-tetrahydropyranyl	2, 4, 6-Me ₃ -Ph
	720	Me	NH-cyclopentyl	2, 4, 6-Me ₃ -Ph
	721	Me	OEt	2, 4, 6-Me ₃ -Ph
	722	Me	OCH(Et)CH ₂ OMe	2, 4, 6-Me ₃ -Ph
10	723	Me	OCH ₂ Ph	2, 4, 6-Me ₃ -Ph
	724	Me	O-3-pentyl	2, 4, 6-Me ₃ -Ph
	725	Me	SEt	2, 4, 6-Me ₃ -Ph
	726	Me	S(O)Et	2, 4, 6-Me ₃ -Ph
	727	Me	SO ₂ Et	2, 4, 6-Me ₃ -Ph
	728	Me	CH(CO ₂ Et) ₂	2, 4, 6-Me ₃ -Ph
15	729	Me	C(Et)(CO ₂ Et) ₂	2, 4, 6-Me ₃ -Ph
	730	Me	CH(Et)CH ₂ OH	2, 4, 6-Me ₃ -Ph
	731	Me	CH(Et)CH ₂ OMe	2, 4, 6-Me ₃ -Ph
	732	Me	CONMe ₂	2, 4, 6-Me ₃ -Ph
	733	Me	COCH ₃	2, 4, 6-Me ₃ -Ph
	734	Me	CH(OH)CH ₃	2, 4, 6-Me ₃ -Ph
20	735	Me	C(OH)Ph-3-pyridyl	2, 4, 6-Me ₃ -Ph
	736	Me	Ph	2, 4, 6-Me ₃ -Ph
	737	Me	2-Ph-Ph	2, 4, 6-Me ₃ -Ph
	738	Me	3-pentyl	2, 4, 6-Me ₃ -Ph
	739	Me	cyclobutyl	2, 4, 6-Me ₃ -Ph
	740	Me	3-pyridyl	2, 4, 6-Me ₃ -Ph
25	741	Me	CH(Et)CH ₂ CONMe ₂	2, 4, 6-Me ₃ -Ph
	742	Me	CH(Et)CH ₂ CH ₂ NMe ₂	2, 4, 6-Me ₃ -Ph
	743	Me	NHCH(CH ₂ OMe) ₂	2, 4-Me ₂ -Ph
	744	Me	N(CH ₂ CH ₂ OMe) ₂	2, 4-Me ₂ -Ph
	745	Me	NHCH(Et)CH ₂ OMe	2, 4-Me ₂ -Ph
	746	Me	NH-3-pentyl	2, 4-Me ₂ -Ph
30	747	Me	NET ₂	2, 4-Me ₂ -Ph
	748	Me	N(CH ₂ CN) ₂	2, 4-Me ₂ -Ph

			NHCH(Me)CH ₂ OMe	2,4-Me ₂ -Ph
			OCH(Et)CH ₂ OMe	2,4-Me ₂ -Ph
			NPr-c-C ₃ H ₅	2,4-Me ₂ -Ph
			NHCH(Me)CH ₂ NMe ₂	2,4-Me ₂ -Ph
5	753	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	754	Me	N(Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	755	Me	N(Bu)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	756	Me	NHCHPr ₂	2,4-Me ₂ -Ph
	757	Me	NEtBu	2,4-Me ₂ -Ph
	10	758	NPr(CH ₂ -c-C ₃ H ₅)	2,4-Me ₂ -Ph
		759	NH-3-heptyl	2,4-Me ₂ -Ph
		760	NET ₂	2,4-Me ₂ -Ph
		761	NHCH(CH ₂ OEt) ₂	2,4-Me ₂ -Ph
		762	NH-3-pentyl	2,4-Me ₂ -Ph
15	763	Me	NMePh	2,4-Me ₂ -Ph
	764	Me	NPr ₂	2,4-Me ₂ -Ph
	765	Me	NH-3-hexyl	2,4-Me ₂ -Ph
	766	Me	morpholino	2,4-Me ₂ -Ph
	767	Me	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2,4-Me ₂ -Ph
20	768	Me	NHCH(CH ₂ Ph)CH ₂ OMe	2,4-Me ₂ -Ph
	769	Me	NH-4-tetrahydropyranyl	2,4-Me ₂ -Ph
	770	Me	NH-cyclopentyl	2,4-Me ₂ -Ph
	771	Me	NHCH(CH ₂ OMe) ₂	2-Me-4-MeO-Ph
	772	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-MeO-Ph
	773	Me	NHCH(Et)CH ₂ OMe	2-Me-4-MeO-Ph
	774	Me	N(Pr)CH ₂ CH ₂ CN	2-Me-4-MeO-Ph
		775	OCH(Et)CH ₂ OMe	2-Me-4-MeO-Ph
		776	NHCH(CH ₂ OMe) ₂	2-Br-4-MeO-Ph
		777	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-MeO-Ph
25	778	Me	NHCH(Et)CH ₂ OMe	2-Br-4-MeO-Ph
	779	Me	N(Pr)CH ₂ CH ₂ CN	2-Br-4-MeO-Ph
	780	Me	OCH(Et)CH ₂ OMe	2-Br-4-MeO-Ph
	781	Me	NHCH(CH ₂ OMe) ₂	2-Me-4-NMe ₂ -Ph
	782	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-NMe ₂ -Ph
30	783	Me	NHCH(Et)CH ₂ OMe	2-Me-4-NMe ₂ -Ph
	784	Me	N(Pr)CH ₂ CH ₂ CN	2-Me-4-NMe ₂ -Ph

	785	Me	OCH (Et) CH ₂ OMe	2-Me-4-NMe ₂ -Ph
	786	Me	NHCH (CH ₂ OMe) 2	2-Br-4-NMe ₂ -Ph
	787	Me	N (CH ₂ CH ₂ OMe) 2	2-Br-4-NMe ₂ -Ph
	788	Me	NHCH (Et) CH ₂ OMe	2-Br-4-NMe ₂ -Ph
5	789	Me	N (Pr) CH ₂ CH ₂ CN	2-Br-4-NMe ₂ -Ph
	790	Me	OCH (Et) CH ₂ OMe	2-Br-4-NMe ₂ -Ph
	791	Me	NHCH (CH ₂ OMe) 2	2-Br-4-i-Pr-Ph
	792	Me	N (CH ₂ CH ₂ OMe) 2	2-Br-4-i-Pr-Ph
	793	Me	NHCH (Et) CH ₂ OMe	2-Br-4-i-Pr-Ph
	794	Me	N (Pr) CH ₂ CH ₂ CN	2-Br-4-i-Pr-Ph
10	795	Me	OCH (Et) CH ₂ OMe	2-Br-4-i-Pr-Ph
	796	Me	NHCH (CH ₂ OMe) 2	2-Br-4-Me-Ph
	797	Me	N (CH ₂ CH ₂ OMe) 2	2-Br-4-Me-Ph
	798	Me	NHCH (Et) CH ₂ OMe	2-Br-4-Me-Ph
	799	Me	N (Pr) CH ₂ CH ₂ CN	2-Br-4-Me-Ph
15	800	Me	OCH (Et) CH ₂ OMe	2-Br-4-Me-Ph
	801	Me	NHCH (CH ₂ OMe) 2	2-Me-4-Br-Ph
	802	Me	N (CH ₂ CH ₂ OMe) 2	2-Me-4-Br-Ph
	803	Me	NHCH (Et) CH ₂ OMe	2-Me-4-Br-Ph
	804	Me	N (Pr) CH ₂ CH ₂ CN	2-Me-4-Br-Ph
20	805	Me	OCH (Et) CH ₂ OMe	2-Me-4-Br-Ph
	806	Me	NHCH (CH ₂ OMe) 2	2-Cl-4, 6-Me ₂ -Ph
	807	Me	N (CH ₂ CH ₂ OMe) 2	2-Cl-4, 6-Me ₂ -Ph
	808	Me	NHCH (CH ₂ OMe) 2	4-Br-2, 6-(Me) ₂ -Ph
	809	Me	N (CH ₂ CH ₂ OMe) 2	4-Br-2, 6-(Me) ₂ -Ph
25	810	Me	NHCH (CH ₂ OMe) 2	4-i-Pr-2-SMe-Ph
	811	Me	N (CH ₂ CH ₂ OMe) 2	4-i-Pr-2-SMe-Ph
	812	Me	NHCH (CH ₂ OMe) 2	2-Br-4-CF ₃ -Ph
	813	Me	N (CH ₂ CH ₂ OMe) 2	2-Br-4-CF ₃ -Ph
	814	Me	NHCH (CH ₂ OMe) 2	2-Br-4, 6-(MeO) ₂ -Ph
30	815	Me	N (CH ₂ CH ₂ OMe) 2	2-Br-4, 6-(MeO) ₂ -Ph
	816	Me	NHCH (CH ₂ OMe) 2	2-Cl-4, 6-(MeO) ₂ -Ph
	817	Me	N (CH ₂ CH ₂ OMe) 2	2-Cl-4, 6-(MeO) ₂ -Ph
	818	Me	NHCH (CH ₂ OMe) 2	2, 6-(Me) ₂ -4-SMe-Ph
	819	Me	N (CH ₂ CH ₂ OMe) 2	2, 6-(Me) ₂ -4-SMe-Ph
35	820	Me	NHCH (CH ₂ OMe) 2	4-(COMe)-2-Br-Ph

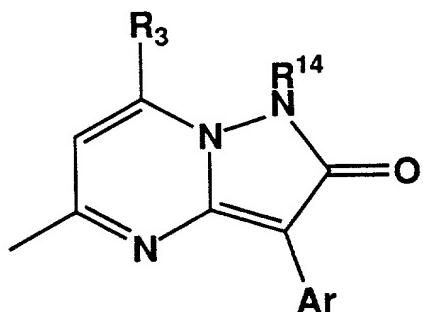
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			N(CH ₂ CH ₂ OMe) ₂	4-(COMe)-2-Br-Ph
			NHCH(CH ₂ OMe) ₂	2,4,6-Me ₃ -pyrid-3-yl
			N(CH ₂ CH ₂ OMe) ₂	2,4,6-Me ₃ -pyrid-3-yl
			NHCH(CH ₂ OMe) ₂	2,4-(Br) ₂ -Ph
5	825	Me	N(CH ₂ CH ₂ OMe) ₂	2,4-(Br) ₂ -Ph
	826	Me	NHCH(CH ₂ OMe) ₂	4-i-Pr-2-SMe-Ph
	827	Me	N(CH ₂ CH ₂ OMe) ₂	4-i-Pr-2-SMe-Ph
	828	Me	NHCH(CH ₂ OMe) ₂	4-i-Pr-2-SO ₂ Me-Ph
	829	Me	N(CH ₂ CH ₂ OMe) ₂	4-i-Pr-2-SO ₂ Me-Ph
	830	Me	NHCH(CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SMe-Ph
10	831	Me	N(CH ₂ CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SMe-Ph
	832	Me	NHCH(CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SO ₂ Me-Ph
	833	Me	N(CH ₂ CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SO ₂ Me-Ph
	834	Me	NHCH(CH ₂ OMe) ₂	2-I-4-i-Pr-Ph
	835	Me	N(CH ₂ CH ₂ OMe) ₂	2-I-4-i-Pr-Ph
	836	Me	NHCH(CH ₂ OMe) ₂	2-Br-4-N(Me) ₂ -6-MeO-Ph
15	837	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-N(Me) ₂ -6-MeO-Ph
	838	Me	NET ₂	2-Br-4-MeO-Ph
	839	Me	NH-3-pentyl	2-Br-4-MeO-Ph
	840	Me	NHCH(CH ₂ OMe) ₂	2-CN-4-Me-Ph
	841	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4,6-Me ₃ -Ph
	842	Me	NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Me-4-Br-Ph
20	843	Me	NHCH(CH ₂ OMe) ₂	2,5-Me ₂ -4-MeO-Ph
	844	Me	N(CH ₂ CH ₂ OMe) ₂	2,5-Me ₂ -4-MeO-Ph
	845	Me	NH-3-pentyl	2,5-Me ₂ -4-MeO-Ph
	846	Me	NET ₂	2,5-Me ₂ -4-MeO-Ph
	847	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MePh
	848	Me	NCH(Et)CH ₂ OMe	2-Cl-4-MePh
25	849	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MePh
	850	Me	(S)-NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Cl-4-MePh
	851	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,5-Me ₂ -4-MeOPh
	852	Me	NET ₂	2-Me-4-MeOPh
	853	Me	OEt	2-Me-4-MeOPh
	854	Me	(S)-NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Me-4-MeOPh
30	855	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2-Me-4-MeOPh
	856	Me	NHCH(CH ₂ CH ₂ OEt) ₂	2-Me-4-MeOPh

			N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4-Cl ₂ -Ph
	857	Me	NET ₂	2-Me-4-ClPh
	858	Me	NH-3-pentyl	2-Me-4-ClPh
	859	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-ClPh
	860	Me	NHCH(CH ₂ OMe) ₂	2-Me-4-ClPh
5	861	Me	NET ₂	2-Me-4-ClPh
	862	Me	NH-3-pentyl	2-Me-4-ClPh
	863	Me	NET ₂	2-Cl-4-MePh
	864	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MePh
	865	Me	NHCH(Et)CH ₂ OMe	2-Cl-4-MeOPh
10	866	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MeOPh
	867	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MeOPh
	868	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4-MeOPh
	869	Me	NET ₂	2-Cl-4-MeOPh
	870	Me	NH-3-pentyl	2-Cl-4-MeOPh
15	871	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
	872	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
	873	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
	874	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
	875	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
20	876	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	877	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4,5-(MeO) ₂ Ph
	878	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,5-(MeO) ₂ Ph
	879	Me	NHCH(Et)CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
	880	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4,5-(MeO) ₂ Ph
25	881	Me	NET ₂	2-Cl-4,5-(MeO) ₂ Ph
	882	Me	NH-3-pentyl	2-Cl-4,5-(MeO) ₂ Ph
	883	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
	884	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4,5-(MeO) ₂ Ph
	885	Me	NHCH(CH ₂ OMe) ₂	2-Br-4,5-(MeO) ₂ Ph
30	886	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4,5-(MeO) ₂ Ph
	887	Me	NHCH(Et)CH ₂ OMe	2-Br-4,5-(MeO) ₂ Ph
	888	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4,5-(MeO) ₂ Ph
	889	Me	NET ₂	2-Br-4,5-(MeO) ₂ Ph
	890	Me	NH-3-pentyl	2-Br-4,5-(MeO) ₂ Ph
35	891	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ Ph
	892	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ Ph

893	Me	NEt ₂	2-Cl-4, 6-(MeO)2Ph	
894	Me	NH-3-pentyl	2-Cl-4, 6-(MeO)2Ph	
895	Me	NHCH(CH ₂ OMe) ₂	2-Me-4, 6-(MeO)2Ph	
896	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4, 6-(MeO)2Ph	
5	897	Me	NHCH(Et)CH ₂ OMe	2-Me-4, 6-(MeO)2Ph
	898	Me	NEt ₂	2-Me-4, 6-(MeO)2Ph
	899	Me	NH-3-pentyl	2-Me-4, 6-(MeO)2Ph
	900	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	901	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
10	902	Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-MePh
	903	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-MePh
	904	Me	NHCH(Et)CH ₂ OMe	2-Me0-4-MePh
	905	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me0-4-MePh
	906	Me	NEt ₂	2-Me0-4-MePh
15	907	Me	NH-3-pentyl	2-Me0-4-MePh
	908	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me0-4-MePh
	909	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me0-4-MePh
	910	Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-MePh
	911	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-MePh
20	912	Me	NHCH(Et)CH ₂ OMe	2-Me0-4-MePh
	913	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me0-4-MePh
	914	Me	NEt ₂	2-Me0-4-MePh
	915	Me	NH-3-pentyl	2-Me0-4-MePh
	916	Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-ClPh
25	917	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-ClPh
	918	Me	NHCH(Et)CH ₂ OMe	2-Me0-4-ClPh
	919	Me	NEt ₂	2-Me0-4-ClPh
	920	Me	NH-3-pentyl	2-Me0-4-ClPh

Table 6



5

	<u>Ex.</u>	<u>R₁₄</u>	<u>R₃</u>	<u>Ar</u>
10	921	Me	NHCH(CH ₂ OMe) ₂	2,4-Cl ₂ -Ph
	922	Me	NHCHPr ₂	2,4-Cl ₂ -Ph
	923	Me	NETBu	2,4-Cl ₂ -Ph
15	924	Me	NPr(CH ₂ -c-C ₃ H ₅)	2,4-Cl ₂ -Ph
	925	Me	N(CH ₂ CH ₂ OMe) ₂	2,4-Cl ₂ -Ph
	926	Me	NH-3-heptyl	2,4-Cl ₂ -Ph
	927	Me	NHCH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph
	928	Me	NET ₂	2,4-Cl ₂ -Ph
20	929	Me	NHCH(CH ₂ OEt) ₂	2,4-Cl ₂ -Ph
	930	Me	NH-3-pentyl	2,4-Cl ₂ -Ph
	931	Me	NMePh	2,4-Cl ₂ -Ph
	932	Me	NPr ₂	2,4-Cl ₂ -Ph
	933	Me	NH-3-hexyl	2,4-Cl ₂ -Ph
25	934	Me	morpholino	2,4-Cl ₂ -Ph
	935	Me	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2,4-Cl ₂ -Ph
	936	Me	NHCH(CH ₂ Ph)CH ₂ OMe	2,4-Cl ₂ -Ph
	937	Me	NH-4-tetrahydropyranyl	2,4-Cl ₂ -Ph
	938	Me	NH-cyclopentyl	2,4-Cl ₂ -Ph
30	939	Me	OEt	2,4-Cl ₂ -Ph
	940	Me	OCH(Et)CH ₂ OMe	2,4-Cl ₂ -Ph
	941	Me	OCH ₂ Ph	2,4-Cl ₂ -Ph
	942	Me	O-3-pentyl	2,4-Cl ₂ -Ph
	943	Me	SEt	2,4-Cl ₂ -Ph

	944	Me	S(O)Et	2,4-Cl ₂ -Ph
	945	Me	SO ₂ Et	2,4-Cl ₂ -Ph
	946	Me	Ph	2,4-Cl ₂ -Ph
	947	Me	2-CF ₃ -Ph	2,4-Cl ₂ -Ph
5	948	Me	2-Ph-Ph	2,4-Cl ₂ -Ph
	949	Me	3-pentyl	2,4-Cl ₂ -Ph
	950	Me	cyclobutyl	2,4-Cl ₂ -Ph
	951	Me	3-pyridyl	2,4-Cl ₂ -Ph
	952	Me	CH(Et)CH ₂ CONMe ₂	2,4-Cl ₂ -Ph
	10	953	CH(Et)CH ₂ CH ₂ NMe ₂	2,4-Cl ₂ -Ph
	954	Me	NHCH(CH ₂ OMe) ₂	2,4,6-Me ₃ -Ph
	955	Me	NHCHPr ₂	2,4,6-Me ₃ -Ph
	956	Me	NETBu	2,4,6-Me ₃ -Ph
	957	Me	NPr(CH ₂ -c-C ₃ H ₅)	2,4,6-Me ₃ -Ph
15	958	Me	N(CH ₂ CH ₂ OMe) ₂	2,4,6-Me ₃ -Ph
	959	Me	NH-3-heptyl	2,4,6-Me ₃ -Ph
	960	Me	NHCH(Et)CH ₂ OMe	2,4,6-Me ₃ -Ph
	961	Me	NET ₂	2,4,6-Me ₃ -Ph
	962	Me	NHCH(CH ₂ OEt) ₂	2,4,6-Me ₃ -Ph
	20	963	NH-3-pentyl	2,4,6-Me ₃ -Ph
	964	Me	NMePh	2,4,6-Me ₃ -Ph
	965	Me	NPr ₂	2,4,6-Me ₃ -Ph
	966	Me	NH-3-hexyl	2,4,6-Me ₃ -Ph
	967	Me	morpholino	2,4,6-Me ₃ -Ph
25	968	Me	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2,4,6-Me ₃ -Ph
	969	Me	NHCH(CH ₂ Ph)CH ₂ OMe	2,4,6-Me ₃ -Ph
	970	Me	NH-4-tetrahydropyranyl	2,4,6-Me ₃ -Ph
	971	Me	NH-cyclopentyl	2,4,6-Me ₃ -Ph
	972	Me	OEt	2,4,6-Me ₃ -Ph
	30	973	OCH(Et)CH ₂ OMe	2,4,6-Me ₃ -Ph
	974	Me	OCH ₂ Ph	2,4,6-Me ₃ -Ph
	975	Me	O-3-pentyl	2,4,6-Me ₃ -Ph
	976	Me	SEt	2,4,6-Me ₃ -Ph
	977	Me	S(O)Et	2,4,6-Me ₃ -Ph
35	978	Me	SO ₂ Et	2,4,6-Me ₃ -Ph
	979	Me	CH(CO ₂ Et) ₂	2,4,6-Me ₃ -Ph

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	980	Me	C(Et)(CO ₂ Et) ₂	2,4,6-Me ₃ -Ph
	981	Me	CH(Et)CH ₂ OH	2,4,6-Me ₃ -Ph
	982	Me	CH(Et)CH ₂ OMe	2,4,6-Me ₃ -Ph
	983	Me	CONMe ₂	2,4,6-Me ₃ -Ph
5	984	Me	COCH ₃	2,4,6-Me ₃ -Ph
	985	Me	CH(OH)CH ₃	2,4,6-Me ₃ -Ph
	986	Me	C(OH)Ph-3-pyridyl	2,4,6-Me ₃ -Ph
	987	Me	Ph	2,4,6-Me ₃ -Ph
	988	Me	2-Ph-Ph	2,4,6-Me ₃ -Ph
	989	Me	3-pentyl	2,4,6-Me ₃ -Ph
10	990	Me	cyclobutyl	2,4,6-Me ₃ -Ph
	991	Me	3-pyridyl	2,4,6-Me ₃ -Ph
	992	Me	CH(Et)CH ₂ CONMe ₂	2,4,6-Me ₃ -Ph
	993	Me	CH(Et)CH ₂ CH ₂ NMe ₂	2,4,6-Me ₃ -Ph
15	994	Me	NHCH(CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	995	Me	N(CH ₂ CH ₂ OMe) ₂	2,4-Me ₂ -Ph
	996	Me	NHCH(Et)CH ₂ OMe	2,4-Me ₂ -Ph
	997	Me	NH-3-pentyl	2,4-Me ₂ -Ph
	998	Me	NET ₂	2,4-Me ₂ -Ph
	999	Me	N(CH ₂ CN) ₂	2,4-Me ₂ -Ph
20	1000	Me	NHCH(Me)CH ₂ OMe	2,4-Me ₂ -Ph
	1001	Me	OCH(Et)CH ₂ OMe	2,4-Me ₂ -Ph
	1002	Me	NPr-c-C ₃ H ₅	2,4-Me ₂ -Ph
	1003	Me	NHCH(Me)CH ₂ NMe ₂	2,4-Me ₂ -Ph
	1004	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
25	1005	Me	N(Pr)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	1006	Me	N(Bu)CH ₂ CH ₂ CN	2,4-Me ₂ -Ph
	1007	Me	NHCHPr ₂	2,4-Me ₂ -Ph
	1008	Me	NETBu	2,4-Me ₂ -Ph
	1009	Me	NPr(CH ₂ -c-C ₃ H ₅)	2,4-Me ₂ -Ph
30	1010	Me	NH-3-heptyl	2,4-Me ₂ -Ph
	1011	Me	NET ₂	2,4-Me ₂ -Ph
	1012	Me	NHCH(CH ₂ OEt) ₂	2,4-Me ₂ -Ph
	1013	Me	NH-3-pentyl	2,4-Me ₂ -Ph
	1014	Me	NMePh	2,4-Me ₂ -Ph
35	1015	Me	NPr ₂	2,4-Me ₂ -Ph

	1016	Me	NH-3-hexyl	2,4-Me ₂ -Ph
	1017	Me	morpholino	2,4-Me ₂ -Ph
	1018	Me	N(CH ₂ Ph)CH ₂ CH ₂ OMe	2,4-Me ₂ -Ph
	1019	Me	NHCH(CH ₂ Ph)CH ₂ OMe	2,4-Me ₂ -Ph
5	1020	Me	NH-4-tetrahydropyranyl	2,4-Me ₂ -Ph
	1021	Me	NH-cyclopentyl	2,4-Me ₂ -Ph
	1022	Me	NHCH(CH ₂ OMe) ₂	2-Me-4-MeO-Ph
	1023	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-MeO-Ph
	1024	Me	NHCH(Et)CH ₂ OMe	2-Me-4-MeO-Ph
	1025	Me	N(Pr)CH ₂ CH ₂ CN	2-Me-4-MeO-Ph
10	1026	Me	OCH(Et)CH ₂ OMe	2-Me-4-MeO-Ph
	1027	Me	NHCH(CH ₂ OMe) ₂	2-Br-4-MeO-Ph
	1028	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-MeO-Ph
	1029	Me	NHCH(Et)CH ₂ OMe	2-Br-4-MeO-Ph
	1030	Me	N(Pr)CH ₂ CH ₂ CN	2-Br-4-MeO-Ph
15	1031	Me	OCH(Et)CH ₂ OMe	2-Br-4-MeO-Ph
	1032	Me	NHCH(CH ₂ OMe) ₂	2-Me-4-NMe ₂ -Ph
	1033	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-NMe ₂ -Ph
	1034	Me	NHCH(Et)CH ₂ OMe	2-Me-4-NMe ₂ -Ph
	1035	Me	N(Pr)CH ₂ CH ₂ CN	2-Me-4-NMe ₂ -Ph
20	1036	Me	OCH(Et)CH ₂ OMe	2-Me-4-NMe ₂ -Ph
	1037	Me	NHCH(CH ₂ OMe) ₂	2-Br-4-NMe ₂ -Ph
	1038	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-NMe ₂ -Ph
	1039	Me	NHCH(Et)CH ₂ OMe	2-Br-4-NMe ₂ -Ph
	1040	Me	N(Pr)CH ₂ CH ₂ CN	2-Br-4-NMe ₂ -Ph
25	1041	Me	OCH(Et)CH ₂ OMe	2-Br-4-NMe ₂ -Ph
	1042	Me	NHCH(CH ₂ OMe) ₂	2-Br-4-i-Pr-Ph
	1043	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-i-Pr-Ph
	1044	Me	NHCH(Et)CH ₂ OMe	2-Br-4-i-Pr-Ph
	1045	Me	N(Pr)CH ₂ CH ₂ CN	2-Br-4-i-Pr-Ph
30	1046	Me	OCH(Et)CH ₂ OMe	2-Br-4-i-Pr-Ph
	1047	Me	NHCH(CH ₂ OMe) ₂	2-Br-4-Me-Ph
	1048	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-Me-Ph
	1049	Me	NHCH(Et)CH ₂ OMe	2-Br-4-Me-Ph
	1050	Me	N(Pr)CH ₂ CH ₂ CN	2-Br-4-Me-Ph
35	1051	Me	OCH(Et)CH ₂ OMe	2-Br-4-Me-Ph

	1052	Me	NHCH(CH ₂ OMe) ₂	2-Me-4-Br-Ph
	1053	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-Br-Ph
	1054	Me	NHCH(Et)CH ₂ OMe	2-Me-4-Br-Ph
	1055	Me	N(Pr)CH ₂ CH ₂ CN	2-Me-4-Br-Ph
5	1056	Me	OCH(Et)CH ₂ OMe	2-Me-4-Br-Ph
	1057	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4,6-Me ₂ -Ph
	1058	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,6-Me ₂ -Ph
	1059	Me	NHCH(CH ₂ OMe) ₂	4-Br-2,6-(Me) ₂ -Ph
	1060	Me	N(CH ₂ CH ₂ OMe) ₂	4-Br-2,6-(Me) ₂ -Ph
	1061	Me	NHCH(CH ₂ OMe) ₂	4-i-Pr-2-SMe-Ph
	1062	Me	N(CH ₂ CH ₂ OMe) ₂	4-i-Pr-2-SMe-Ph
10	1063	Me	NHCH(CH ₂ OMe) ₂	2-Br-4-CF ₃ -Ph
	1064	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-CF ₃ -Ph
	1065	Me	NHCH(CH ₂ OMe) ₂	2-Br-4,6-(MeO) ₂ -Ph
	1066	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4,6-(MeO) ₂ -Ph
	1067	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ -Ph
15	1068	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,6-(MeO) ₂ -Ph
	1069	Me	NHCH(CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SMe-Ph
	1070	Me	N(CH ₂ CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SMe-Ph
	1071	Me	NHCH(CH ₂ OMe) ₂	4-(COMe)-2-Br-Ph
	1072	Me	N(CH ₂ CH ₂ OMe) ₂	4-(COMe)-2-Br-Ph
20	1073	Me	NHCH(CH ₂ OMe) ₂	2,4,6-Me ₃ -pyrid-3-yl
	1074	Me	N(CH ₂ CH ₂ OMe) ₂	2,4,6-Me ₃ -pyrid-3-yl
	1075	Me	NHCH(CH ₂ OMe) ₂	2,4-(Br) ₂ -Ph
	1076	Me	N(CH ₂ CH ₂ OMe) ₂	2,4-(Br) ₂ -Ph
	1077	Me	NHCH(CH ₂ OMe) ₂	4-i-Pr-2-SMe-Ph
25	1078	Me	N(CH ₂ CH ₂ OMe) ₂	4-i-Pr-2-SMe-Ph
	1079	Me	NHCH(CH ₂ OMe) ₂	4-i-Pr-2-SO ₂ Me-Ph
	1080	Me	N(CH ₂ CH ₂ OMe) ₂	4-i-Pr-2-SO ₂ Me-Ph
	1081	Me	NHCH(CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SMe-Ph
	1082	Me	N(CH ₂ CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SMe-Ph
30	1083	Me	NHCH(CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SO ₂ Me-Ph
	1084	Me	N(CH ₂ CH ₂ OMe) ₂	2,6-(Me) ₂ -4-SO ₂ Me-Ph
	1085	Me	NHCH(CH ₂ OMe) ₂	2-I-4-i-Pr-Ph
	1086	Me	N(CH ₂ CH ₂ OMe) ₂	2-I-4-i-Pr-Ph
	1087	Me	NHCH(CH ₂ OMe) ₂	2-Br-4-N(Me) ₂ -6-MeO-Ph

	1088	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4-N(Me)2-6-MeO-Ph
	1089	Me	NET ₂	2-Br-4-MeO-Ph
	1090	Me	NH-3-pentyl	2-Br-4-MeO-Ph
	1091	Me	NHCH(CH ₂ OMe) ₂	2-CN-4-Me-Ph
5	1092	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4,6-Me ₃ -Ph
	1093	Me	NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Me-4-Br-Ph
	1094	Me	NHCH(CH ₂ OMe) ₂	2,5-Me ₂ -4-MeO-Ph
	1095	Me	N(CH ₂ CH ₂ OMe) ₂	2,5-Me ₂ -4-MeO-Ph
	1096	Me	NH-3-pentyl	2,5-Me ₂ -4-MeO-Ph
	1097	Me	NET ₂	2,5-Me ₂ -4-MeO-Ph
10	1098	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MePh
	1099	Me	NCH(Et)CH ₂ OMe	2-Cl-4-MePh
	1100	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MePh
	1101	Me	(S)-NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Cl-4-MePh
	1102	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,5-Me ₂ -4-MeOPh
	1103	Me	NET ₂	2-Me-4-MeOPh
15	1104	Me	OEt	2-Me-4-MeOPh
	1105	Me	(S)-NHCH(CH ₂ CH ₂ OMe)CH ₂ OMe	2-Me-4-MeOPh
	1106	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2-Me-4-MeOPh
	1107	Me	NHCH(CH ₂ CH ₂ OEt) ₂	2-Me-4-MeOPh
	1108	Me	N(c-C ₃ H ₅)CH ₂ CH ₂ CN	2,4-Cl ₂ -Ph
	1109	Me	NET ₂	2-Me-4-ClPh
20	1110	Me	NH-3-pentyl	2-Me-4-ClPh
	1111	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4-ClPh
	1112	Me	NHCH(CH ₂ OMe) ₂	2-Me-4-ClPh
	1113	Me	NET ₂	2-Me-4-ClPh
	1114	Me	NET ₂	2-Cl-4-MePh
	1115	Me	NH-3-pentyl	2-Cl-4-MePh
25	1116	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4-MeOPh
	1117	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4-MeOPh
	1118	Me	NHCH(Et)CH ₂ OMe	2-Cl-4-MeOPh
	1119	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4-MeOPh
	1120	Me	NET ₂	2-Cl-4-MeOPh
	1121	Me	NH-3-pentyl	2-Cl-4-MeOPh
30	1123	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh
	1124	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4-MeOPh

	1125	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
	1126	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Br-4-MeOPh
	1127	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	1128	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
5	1129	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4,5-(MeO)2Ph
	1130	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,5-(MeO)2Ph
	1131	Me	NHCH(Et)CH ₂ OMe	2-Cl-4,5-(MeO)2Ph
	1132	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Cl-4,5-(MeO)2Ph
	1133	Me	NET ₂	2-Cl-4,5-(MeO)2Ph
10	1134	Me	NH-3-pentyl	2-Cl-4,5-(MeO)2Ph
	1135	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Cl-4,5-(MeO)2Ph
	1136	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Cl-4,5-(MeO)2Ph
	1137	Me	NHCH(CH ₂ OMe) ₂	2-Br-4,5-(MeO)2Ph
	1138	Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4,5-(MeO)2Ph
15	1139	Me	NHCH(Et)CH ₂ OMe	2-Br-4,5-(MeO)2Ph
	1140	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Br-4,5-(MeO)2Ph
	1141	Me	NET ₂	2-Br-4,5-(MeO)2Ph
	1142	Me	NH-3-pentyl	2-Br-4,5-(MeO)2Ph
	1143	Me	NHCH(CH ₂ OMe) ₂	2-Cl-4,6-(MeO)2Ph
20	1144	Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,6-(MeO)2Ph
	1145	Me	NET ₂	2-Cl-4,6-(MeO)2Ph
	1146	Me	NH-3-pentyl	2-Cl-4,6-(MeO)2Ph
	1147	Me	NHCH(CH ₂ OMe) ₂	2-Me-4,6-(MeO)2Ph
	1148	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me-4,6-(MeO)2Ph
25	1149	Me	NHCH(Et)CH ₂ OMe	2-Me-4,6-(MeO)2Ph
	1150	Me	NET ₂	2-Me-4,6-(MeO)2Ph
	1151	Me	NH-3-pentyl	2-Me-4,6-(MeO)2Ph
	1152	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
	1153	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-Me-4-MeOPh
30	1154	Me	NHCH(CH ₂ OMe) ₂	2-Me0-4-MePh
	1155	Me	N(CH ₂ CH ₂ OMe) ₂	2-Me0-4-MePh
	1156	Me	NHCH(Et)CH ₂ OMe	2-Me0-4-MePh
	1157	Me	N(c-Pr)CH ₂ CH ₂ CN	2-Me0-4-MePh
	1158	Me	NET ₂	2-Me0-4-MePh
35	1159	Me	NH-3-pentyl	2-Me0-4-MePh
	1160	Me	NHCH(Et)CH ₂ CH ₂ OMe	2-Me0-4-MePh

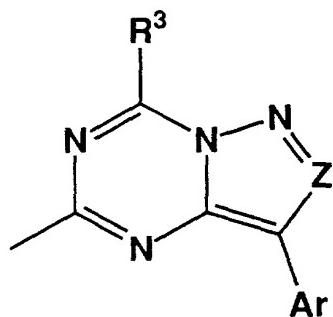
	1161	Me	NHCH(Me)CH ₂ CH ₂ OMe	2-MeO-4-MePh
	1162	Me	NHCH(CH ₂ OMe) ₂	2-MeO-4-MePh
	1163	Me	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-MePh
	1164	Me	NHCH(Et)CH ₂ OMe	2-MeO-4-MePh
5	1165	Me	N(c-Pr)CH ₂ CH ₂ CN	2-MeO-4-MePh
	1166	Me	NET ₂	2-MeO-4-MePh
	1167	Me	NH-3-pentyl	2-MeO-4-MePh
	1168	Me	NHCH(CH ₂ OMe) ₂	2-MeO-4-ClPh
	1169	Me	N(CH ₂ CH ₂ OMe) ₂	2-MeO-4-ClPh
10	1170	Me	NHCH(Et)CH ₂ OMe	2-MeO-4-ClPh
	1171	Me	NET ₂	2-MeO-4-ClPh
	1172	Me	NH-3-pentyl	2-MeO-4-ClPh

15

The examples delineated in Table 7 may be prepared by the methods outlined in Examples 1, 2, 3 or 6. Commonly used abbreviations are: Ph is phenyl, Pr is propyl, Me is methyl, Et is ethyl, Bu is butyl, Ex is Example.

20

Table 7



	Ex.	Z	R ₃	Ar	mp (°C)
25	1200a	C-Me	2-ethylpiperidyl	2-Me-4-OMePh	58-59.5
	1201b	C-Me	cyclobutylamino	2-Me-4-OMePh	94.5-96
	1202c	C-Me	N(Me)CH ₂ CH=CH ₂	2-Me-4-OMePh	oil
	1203d	C-Me	N(CH ₂ CH=CH ₂) ₂	2-Me-4-OMePh	oil
30	1204	C-Me	N(Et)CH ₂ C-Pr	2-Me-4-OMePh	

	1205e	C-Me	NHCH ₂ -2-tetrahydrofuryl	2-Me-4-OMePh	amorphous
	1206	C-Me	N(Pr)CH ₂ c-Pr	2-Me-4-OMePh	
	1207	C-Me	N(Me) Pr	2-Me-4-OMePh	
	1208f	C-Me	N(Me) Et	2-Me-4-OMePh	oil
5	1209g	C-Me	N(Me) Bu	2-Me-4-OMePh	oil
	1210h	C-Me	N(Me) propargyl	2-Me-4-OMePh	oil
	1211i	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Me-4-OMePh	oil
	1212j	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Me-4-OMePh	oil
	1213k	C-Me	N(CH ₂ CH ₂ OMe) Me	2-Me-4-OMePh	oil
10	1214	C-Me	N(CH ₂ CH ₂ OMe) Et	2-Me-4-OMePh	
	1215	C-Me	N(CH ₂ CH ₂ OMe) Pr	2-Me-4-OMePh	
	1216	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2-Me-4-OMePh	
	1217m	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Me-4-OMePh	oil
	1218	C-Me	NHCH(c-Pr) ₂	2-Me-4-OMePh	
15	1219n	C-Me	NH-2-hexyl	2-Me-4-OMePh	oil
	1220o	C-Me	NH-2-propyl	2-Me-4-OMePh	oil
	1221p	C-Me	NHCH ₂ -2-tetrahydrofuryl	2-Me-4-OMePh	amorphous
	1222q	C-Me	NET(cyclohexyl)	2-Me-4-OMePh	oil
	1223	C-Me	2-ethylpiperidyl	2,5-Me ₂ -4-OMePh	
20	1224	C-Me	cyclobutylamino	2,5-Me ₂ -4-OMePh	
	1225	C-Me	N(Me)CH ₂ CH=CH ₂	2,5-Me ₂ -4-OMePh	
	1226	C-Me	N(Et)CH ₂ c-Pr	2,5-Me ₂ -4-OMePh	
	1227	C-Me	N(Pr)CH ₂ c-Pr	2,5-Me ₂ -4-OMePh	
	1228	C-Me	N(Me) Pr	2,5-Me ₂ -4-OMePh	
25	1229	C-Me	N(Me) Et	2,5-Me ₂ -4-OMePh	
	1230	C-Me	N(Me) Bu	2,5-Me ₂ -4-OMePh	
	1231	C-Me	N(Me) propargyl	2,5-Me ₂ -4-OMePh	
	1232	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2,5-Me ₂ -4-OMePh	
	1233	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2,5-Me ₂ -4-OMePh	
30	1234	C-Me	N(CH ₂ CH ₂ OMe) Me	2,5-Me ₂ -4-OMePh	
	1235	C-Me	N(CH ₂ CH ₂ OMe) Et	2,5-Me ₂ -4-OMePh	
	1236	C-Me	N(CH ₂ CH ₂ OMe) Pr	2,5-Me ₂ -4-OMePh	
	1237	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2,5-Me ₂ -4-OMePh	
	1238	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2,5-Me ₂ -4-OMePh	
35	1239	C-Me	NHCH(c-Pr) ₂	2,5-Me ₂ -4-OMePh	

	1240	C-Me	2-ethylpiperidyl	2, 4-(OMe)2Ph	
	1241	C-Me	cyclobutylamino	2, 4-(OMe)2Ph	
	1245	C-Me	N(Me)CH ₂ CH=CH ₂	2, 4-(OMe)2Ph	
	1255^r	C-Me	N(CH ₂ CH=CH ₂) ₂	2, 4-(OMe)2Ph	64.8-65.6
5	1256	C-Me	N(Et)CH ₂ C-Pr	2, 4-(OMe)2Ph	
	1257	C-Me	N(Pr)CH ₂ C-Pr	2, 4-(OMe)2Ph	
	1258	C-Me	N(Me)Pr	2, 4-(OMe)2Ph	
	1259	C-Me	N(Me)Et	2, 4-(OMe)2Ph	
	1260	C-Me	N(Me)Bu	2, 4-(OMe)2Ph	
10	1261	C-Me	N(Me)propargyl	2, 4-(OMe)2Ph	
	1262	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2, 4-(OMe)2Ph	
	1263	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2, 4-(OMe)2Ph	
	1264	C-Me	N(CH ₂ CH ₂ OMe)Me	2, 4-(OMe)2Ph	
	1265	C-Me	N(CH ₂ CH ₂ OMe)Et	2, 4-(OMe)2Ph	
15	1266	C-Me	N(CH ₂ CH ₂ OMe)Pr	2, 4-(OMe)2Ph	
	1267	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2, 4-(OMe)2Ph	
	1268^s	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2, 4-(OMe)2Ph	137.8-138.3
	1269	C-Me	NHCH(C-Pr) ₂	2, 4-(OMe)2Ph	
	1270^t	C-Me	N(CH ₂ CH ₂ OMe) ₂	2, 4-(OMe)2Ph	oil
20	1271^u	C-Me	NHCH(Et) ₂	2, 4-(OMe)2Ph	128-129.4
	1272	C-Me	N(Et) ₂	2, 4-(OMe)2Ph	
	1273^v	C-Me	N(Pr) ₂	2, 4-(OMe)2Ph	
	1274	C-Me	2-ethylpiperidyl	2, 4-(OMe)2-5-MePh	
	1275	C-Me	cyclobutylamino	2, 4-(OMe)2-5-MePh	
25	1276	C-Me	N(Me)CH ₂ CH=CH ₂	2, 4-(OMe)2-5-MePh	
	1277	C-Me	N(Et)CH ₂ C-Pr	2, 4-(OMe)2-5-MePh	
	1278	C-Me	N(Pr)CH ₂ C-Pr	2, 4-(OMe)2-5-MePh	
	1279	C-Me	N(Me)Pr	2, 4-(OMe)2-5-MePh	
	1280	C-Me	N(Me)Et	2, 4-(OMe)2-5-MePh	
30	1281	C-Me	N(Me)Bu	2, 4-(OMe)2-5-MePh	
	1282	C-Me	N(Me)propargyl	2, 4-(OMe)2-5-MePh	
	1283	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2, 4-(OMe)2-5-MePh	
	1284	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2, 4-(OMe)2-5-MePh	
	1285	C-Me	N(CH ₂ CH ₂ OMe)Me	2, 4-(OMe)2-5-MePh	
35	1286	C-Me	N(CH ₂ CH ₂ OMe)Et	2, 4-(OMe)2-5-MePh	

	1287	C-Me	N(CH ₂ CH ₂ OMe)Pr	2, 4-(OMe) ₂ -5-MePh
	1288	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2, 4-(OMe) ₂ -5-MePh
	1289	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2, 4-(OMe) ₂ -5-MePh
	1290	C-Me	NHCH(c-Pr) ₂	2, 4-(OMe) ₂ -5-MePh
5	1291	C-Me	N(CH ₂ CH ₂ OMe) ₂	2, 4-(OMe) ₂ -5-MePh
	1292	C-Me	NHCH(Et) ₂	2, 4-(OMe) ₂ -5-MePh
	1293	C-Me	N(Et) ₂	2, 4-(OMe) ₂ -5-MePh
	1294	C-Me	2-ethylpiperidyl	2, 4-(OMe) ₂ -5-ClPh
	1295	C-Me	cyclobutylamino	2, 4-(OMe) ₂ -5-ClPh
	10	1296	C-Me	N(Me)CH ₂ CH=CH ₂
	1297	C-Me	N(Et)CH ₂ c-Pr	2, 4-(OMe) ₂ -5-ClPh
	1298	C-Me	N(Pr)CH ₂ c-Pr	2, 4-(OMe) ₂ -5-ClPh
	1299	C-Me	N(Me)Pr	2, 4-(OMe) ₂ -5-ClPh
	1300	C-Me	N(Me)Et	2, 4-(OMe) ₂ -5-ClPh
15	1301	C-Me	N(Me)Bu	2, 4-(OMe) ₂ -5-ClPh
	1302	C-Me	N(Me)propargyl	2, 4-(OMe) ₂ -5-ClPh
	1303	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2, 4-(OMe) ₂ -5-ClPh
	1304	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2, 4-(OMe) ₂ -5-ClPh
	1305	C-Me	N(CH ₂ CH ₂ OMe)Me	2, 4-(OMe) ₂ -5-ClPh
20	1306	C-Me	N(CH ₂ CH ₂ OMe)Et	2, 4-(OMe) ₂ -5-ClPh
	1307	C-Me	N(CH ₂ CH ₂ OMe)Pr	2, 4-(OMe) ₂ -5-ClPh
	1308	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2, 4-(OMe) ₂ -5-ClPh
	1309	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2, 4-(OMe) ₂ -5-ClPh
	1310	C-Me	NHCH(c-Pr) ₂	2, 4-(OMe) ₂ -5-ClPh
25	1311	C-Me	N(CH ₂ CH ₂ OMe) ₂	2, 4-(OMe) ₂ -5-ClPh
	1312	C-Me	NHCH(Et) ₂	2, 4-(OMe) ₂ -5-ClPh
	1313	C-Me	N(Et) ₂	2, 4-(OMe) ₂ -5-ClPh
	1314	C-Me	2-ethylpiperidyl	2-Me-4, 6-(OMe) ₂ Ph
	1315	C-Me	cyclobutylamino	2-Me-4, 6-(OMe) ₂ Ph
30	1316	C-Me	N(Me)CH ₂ CH=CH ₂	2-Me-4, 6-(OMe) ₂ Ph
	1317	C-Me	N(Et)CH ₂ c-Pr	2-Me-4, 6-(OMe) ₂ Ph
	1318	C-Me	N(Pr)CH ₂ c-Pr	2-Me-4, 6-(OMe) ₂ Ph
	1319	C-Me	N(Me)Pr	2-Me-4, 6-(OMe) ₂ Ph
	1320	C-Me	N(Me)Et	2-Me-4, 6-(OMe) ₂ Ph
35	1321	C-Me	N(Me)Bu	2-Me-4, 6-(OMe) ₂ Ph

	1322	C-Me	N(Me) propargyl	2-Me-4, 6-(OMe) 2Ph
	1323	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Me-4, 6-(OMe) 2Ph
	1324	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Me-4, 6-(OMe) 2Ph
	1325	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Me-4, 6-(OMe) 2Ph
5	1326	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Me-4, 6-(OMe) 2Ph
	1327	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Me-4, 6-(OMe) 2Ph
	1328	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2-Me-4, 6-(OMe) 2Ph
	1329	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Me-4, 6-(OMe) 2Ph
	1330	C-Me	NHCH(c-Pr) ₂	2-Me-4, 6-(OMe) 2Ph
	10	1331^w	C-Me	N(CH ₂ CH ₂ OMe) ₂
	1332	C-Me	NHCH(Et) ₂	2-Me-4, 6-(OMe) 2Ph
	1333	C-Me	N(Et) ₂	2-Me-4, 6-(OMe) 2Ph
	1334^x	C-Me	NET(Bu)	2-Me-4, 6-(OMe) 2Ph
	1335	C-Me	2-ethylpiperidyl	2-Cl-4, 6-(OMe) 2Ph
15	1336	C-Me	cyclobutylamino	2-Cl-4, 6-(OMe) 2Ph
	1337	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-4, 6-(OMe) 2Ph
	1338	C-Me	N(Et)CH ₂ c-Pr	2-Cl-4, 6-(OMe) 2Ph
	1339	C-Me	N(Pr)CH ₂ c-Pr	2-Cl-4, 6-(OMe) 2Ph
	1340	C-Me	N(Me)Pr	2-Cl-4, 6-(OMe) 2Ph
	20	1341	C-Me	N(Me)Et
	1342	C-Me	N(Me)Bu	2-Cl-4, 6-(OMe) 2Ph
	1343	C-Me	N(Me) propargyl	2-Cl-4, 6-(OMe) 2Ph
	1344	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-4, 6-(OMe) 2Ph
	1345	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-4, 6-(OMe) 2Ph
25	1346	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-4, 6-(OMe) 2Ph
	1347	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-4, 6-(OMe) 2Ph
	1348	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4, 6-(OMe) 2Ph
	1349	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2-Cl-4, 6-(OMe) 2Ph
	1350	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4, 6-(OMe) 2Ph
	30	1351	C-Me	NHCH(c-Pr) ₂
	1352	C-Me	NHCH(Et) ₂	2-Cl-4, 6-(OMe) 2Ph
	1353	C-Me	N(Et) ₂	2-Cl-4, 6-(OMe) 2Ph
	1354	C-Me	2-ethylpiperidyl	2-Cl-4-OMe-Ph
	1355	C-Me	cyclobutylamino	2-Cl-4-OMe-Ph
35	1356	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-4-OMe-Ph

	1357	C-Me	N (Et) CH ₂ C-Pr	2-Cl-4-OMe-Ph
	1358	C-Me	N (Pr) CH ₂ C-Pr	2-Cl-4-OMe-Ph
	1359	C-Me	N (Me) Pr	2-Cl-4-OMe-Ph
	1360	C-Me	N (Me) Et	2-Cl-4-OMe-Ph
5	1361	C-Me	N (Me) Bu	2-Cl-4-OMe-Ph
	1362	C-Me	N (Me) propargyl	2-Cl-4-OMe-Ph
	1363	C-Me	NH (CH (CH ₃) CH (CH ₃) CH ₃)	2-Cl-4-OMe-Ph
	1364	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	2-Cl-4-OMe-Ph
	1365	C-Me	N (CH ₂ CH ₂ OMe) Me	2-Cl-4-OMe-Ph
	1366	C-Me	N (CH ₂ CH ₂ OMe) Et	2-Cl-4-OMe-Ph
10	1367	C-Me	N (CH ₂ CH ₂ OMe) Pr	2-Cl-4-OMe-Ph
	1368	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	2-Cl-4-OMe-Ph
	1369	C-Me	NH (CH (CH ₃) CH ₂ CH ₃)	2-Cl-4-OMe-Ph
	1370	C-Me	NHCH (c-Pr) ₂	2-Cl-4-OMe-Ph
	1371	C-Me	2-ethylpiperidyl	2-Me-4, 5-(OMe) 2Ph
15	1372	C-Me	cyclobutylamino	2-Me-4, 5-(OMe) 2Ph
	1373	C-Me	N (Me) CH ₂ CH=CH ₂	2-Me-4, 5-(OMe) 2Ph
	1374	C-Me	N (Et) CH ₂ C-Pr	2-Me-4, 5-(OMe) 2Ph
	1375	C-Me	N (Pr) CH ₂ C-Pr	2-Me-4, 5-(OMe) 2Ph
	1376	C-Me	N (Me) Pr	2-Me-4, 5-(OMe) 2Ph
20	1377	C-Me	N (Me) Et	2-Me-4, 5-(OMe) 2Ph
	1378	C-Me	N (Me) Bu	2-Me-4, 5-(OMe) 2Ph
	1379	C-Me	N (Me) propargyl	2-Me-4, 5-(OMe) 2Ph
	1380	C-Me	NH (CH (CH ₃) CH (CH ₃) CH ₃)	2-Me-4, 5-(OMe) 2Ph
	1381	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	2-Me-4, 5-(OMe) 2Ph
25	1382	C-Me	N (CH ₂ CH ₂ OMe) Me	2-Me-4, 5-(OMe) 2Ph
	1383	C-Me	N (CH ₂ CH ₂ OMe) Et	2-Me-4, 5-(OMe) 2Ph
	1384	C-Me	N (CH ₂ CH ₂ OMe) Pr	2-Me-4, 5-(OMe) 2Ph
	1385	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	2-Me-4, 5-(OMe) 2Ph
	1386	C-Me	NH (CH (CH ₃) CH ₂ CH ₃)	2-Me-4, 5-(OMe) 2Ph
30	1387	C-Me	NHCH (c-Pr) ₂	2-Me-4, 5-(OMe) 2Ph
	1388	C-Me	N (CH ₂ CH ₂ OMe) ₂	2-Me-4, 5-(OMe) 2Ph
	1389	C-Me	NHCH (Et) ₂	2-Me-4, 5-(OMe) 2Ph
	1390	C-Me	N (Et) ₂	2-Me-4, 5-(OMe) 2Ph
	1391	C-Me	NET (Bu)	2-Me-4, 5-(OMe) 2Ph

	1392	C-Me	2-ethylpiperidyl	2-Cl-4,5-(OMe)2Ph
	1393	C-Me	cyclobutylamino	2-Cl-4,5-(OMe)2Ph
	1394	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-4,5-(OMe)2Ph
	1395	C-Me	N(Et)CH ₂ C-Pr	2-Cl-4,5-(OMe)2Ph
5	1396	C-Me	N(Pr)CH ₂ C-Pr	2-Cl-4,5-(OMe)2Ph
	1397	C-Me	N(Me)Pr	2-Cl-4,5-(OMe)2Ph
	1398	C-Me	N(Me)Et	2-Cl-4,5-(OMe)2Ph
	1399	C-Me	N(Me)Bu	2-Cl-4,5-(OMe)2Ph
	1400	C-Me	N(Me)propargyl	2-Cl-4,5-(OMe)2Ph
	10	1401	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)
	1402	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-4,5-(OMe)2Ph
	1403	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-4,5-(OMe)2Ph
	1404	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-4,5-(OMe)2Ph
	1405	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4,5-(OMe)2Ph
15	1406	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Cl-4,5-(OMe)2Ph
	1407	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4,5-(OMe)2Ph
	1408	C-Me	NHCH(c-Pr) ₂	2-Cl-4,5-(OMe)2Ph
	1409	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Cl-4,5-(OMe)2Ph
	1410	C-Me	NHCH(Et) ₂	2-Cl-4,5-(OMe)2Ph
20	1411	C-Me	N(Et) ₂	2-Cl-4,5-(OMe)2Ph
	1412	C-Me	NET(Bu)	2-Cl-4,5-(OMe)2Ph
	1413	C-Me	2-ethylpiperidyl	2-Cl-4-OMe-5-MePh
	1414	C-Me	cyclobutylamino	2-Cl-4-OMe-5-MePh
	1415	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-4-OMe-5-MePh
	1416	C-Me	N(Et)CH ₂ C-Pr	2-Cl-4-OMe-5-MePh
25	1417	C-Me	N(Pr)CH ₂ C-Pr	2-Cl-4-OMe-5-MePh
	1418	C-Me	N(Me)Pr	2-Cl-4-OMe-5-MePh
	1419	C-Me	N(Me)Et	2-Cl-4-OMe-5-MePh
	1420	C-Me	N(Me)Bu	2-Cl-4-OMe-5-MePh
	30	1421	C-Me	N(Me)propargyl
	1422	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-4-OMe-5-MePh
	1423	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-4-OMe-5-MePh
	1424	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-4-OMe-5-MePh
	1425	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-4-OMe-5-MePh
35	1426	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4-OMe-5-MePh

	1427	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Cl-4-OMe-5-MePh
	1428	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4-OMe-5-MePh
	1429	C-Me	NHCH(C-Pr) ₂	2-Cl-4-OMe-5-MePh
	1430	C-Me	NHCH(Et) ₂	2-Cl-4-OMe-5-MePh
5	1431	C-Me	N(Et) ₂	2-Cl-4-OMe-5-MePh
	1432	C-Me	NET(Bu)	2-Cl-4-OMe-5-MePh
	1433	C-Me	2-ethylpiperidyl	2-Cl-6-OMe-4-MePh
	1434	C-Me	cyclobutylamino	2-Cl-6-OMe-4-MePh
	1435	C-Me	N(Me)CH ₂ CH=CH ₂	2-Cl-6-OMe-4-MePh
10	1436	C-Me	N(Et)CH ₂ C-Pr	2-Cl-6-OMe-4-MePh
	1437	C-Me	N(Pr)CH ₂ C-Pr	2-Cl-6-OMe-4-MePh
	1438	C-Me	N(Me)Pr	2-Cl-6-OMe-4-MePh
	1439	C-Me	N(Me)Et	2-Cl-6-OMe-4-MePh
	1440	C-Me	N(Me)Bu	2-Cl-6-OMe-4-MePh
15	1441	C-Me	N(Me)propargyl	2-Cl-6-OMe-4-MePh
	1442	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-6-OMe-4-MePh
	1443	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-6-OMe-4-MePh
	1444	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-6-OMe-4-MePh
	1445	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-6-OMe-4-MePh
20	1446	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-6-OMe-4-MePh
	1447	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Cl-6-OMe-4-MePh
	1448	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-6-OMe-4-MePh
	1449	C-Me	NHCH(C-Pr) ₂	2-Cl-6-OMe-4-MePh
	1450	C-Me	NHCH(Et) ₂	2-Cl-6-OMe-4-MePh
25	1451	C-Me	N(Et) ₂	2-Cl-6-OMe-4-MePh
	1452	C-Me	NET(Bu)	2-Cl-6-OMe-4-MePh
	1453	C-Me	2-ethylpiperidyl	2,6-Me ₂ -4-OMePh
	1454	C-Me	cyclobutylamino	2,6-Me ₂ -4-OMePh
	1455	C-Me	N(Me)CH ₂ CH=CH ₂	2,6-Me ₂ -4-OMePh
30	1456	C-Me	N(Et)CH ₂ C-Pr	2,6-Me ₂ -4-OMePh
	1457	C-Me	N(Pr)CH ₂ C-Pr	2,6-Me ₂ -4-OMePh
	1458	C-Me	N(Me)Pr	2,6-Me ₂ -4-OMePh
	1459	C-Me	N(Me)Et	2,6-Me ₂ -4-OMePh
	1460	C-Me	N(Me)Bu	2,6-Me ₂ -4-OMePh
35	1461	C-Me	N(Me)propargyl	2,6-Me ₂ -4-OMePh

	1462	C-Me	NH (CH (CH ₃) CH (CH ₃) CH ₃)	2, 6-Me ₂ -4-OMePh	
	1463	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	2, 6-Me ₂ -4-OMePh	
	1464	C-Me	N (CH ₂ CH ₂ OMe) Me	2, 6-Me ₂ -4-OMePh	
	1465	C-Me	N (CH ₂ CH ₂ OMe) Et	2, 6-Me ₂ -4-OMePh	
5	1466	C-Me	N (CH ₂ CH ₂ OMe) Pr	2, 6-Me ₂ -4-OMePh	
	1467	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	2, 6-Me ₂ -4-OMePh	
	1468	C-Me	NH (CH (CH ₃) CH ₂ CH ₃)	2, 6-Me ₂ -4-OMePh	
	1469	C-Me	NHCH (c-Pr) ₂	2, 6-Me ₂ -4-OMePh	
	1470	C-Me	NHCH (Et) ₂	2, 6-Me ₂ -4-OMePh	
	10	1471	C-Me	N (Et) ₂	2, 6-Me ₂ -4-OMePh
		1472	C-Me	NEt (Bu)	2, 6-Me ₂ -4-OMePh
	1473	C-Me	2-ethylpiperidyl	2-Cl-4-OMe-5-FPh	
	1474	C-Me	cyclobutylamino	2-Cl-4-OMe-5-FPh	
	1475	C-Me	N (Me) CH ₂ CH=CH ₂	2-Cl-4-OMe-5-FPh	
15	1476	C-Me	N (Et) CH ₂ C-Pr	2-Cl-4-OMe-5-FPh	
	1478	C-Me	N (Pr) CH ₂ C-Pr	2-Cl-4-OMe-5-FPh	
	1479	C-Me	N (Me) Pr	2-Cl-4-OMe-5-FPh	
	1480	C-Me	N (Me) Et	2-Cl-4-OMe-5-FPh	
	1481	C-Me	N (Me) Bu	2-Cl-4-OMe-5-FPh	
	20	1482	C-Me	N (Me) propargyl	2-Cl-4-OMe-5-FPh
	1483	C-Me	NH (CH (CH ₃) CH (CH ₃) CH ₃)	2-Cl-4-OMe-5-FPh	
	1484	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	2-Cl-4-OMe-5-FPh	
	1485	C-Me	N (CH ₂ CH ₂ OMe) Me	2-Cl-4-OMe-5-FPh	
	1486	C-Me	N (CH ₂ CH ₂ OMe) Et	2-Cl-4-OMe-5-FPh	
25	1487	C-Me	N (CH ₂ CH ₂ OMe) Pr	2-Cl-4-OMe-5-FPh	
	1488	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	2-Cl-4-OMe-5-FPh	
	1489	C-Me	NH (CH (CH ₃) CH ₂ CH ₃)	2-Cl-4-OMe-5-FPh	
	1490	C-Me	NHCH (c-Pr) ₂	2-Cl-4-OMe-5-FPh	
	1491	C-Me	NHCH (Et) ₂	2-Cl-4-OMe-5-FPh	
30	1492	C-Me	N (Et) ₂	2-Cl-4-OMe-5-FPh	
	1493	C-Me	NEt (Bu)	2-Cl-4-OMe-5-FPh	
	1494	C-Me	2-ethylpiperidyl	2-Cl-4-OMe-6-MePh	
	1495	C-Me	cyclobutylamino	2-Cl-4-OMe-6-MePh	
	1496	C-Me	N (Me) CH ₂ CH=CH ₂	2-Cl-4-OMe-6-MePh	
35	1497	C-Me	N (Et) CH ₂ C-Pr	2-Cl-4-OMe-6-MePh	

	1498	C-Me	N(Pr)CH ₂ C-Pr	2-Cl-4-OMe-6-MePh
	1499	C-Me	N(Me)Pr	2-Cl-4-OMe-6-MePh
	1500	C-Me	N(Me)Et	2-Cl-4-OMe-6-MePh
	1501	C-Me	N(Me)Bu	2-Cl-4-OMe-6-MePh
5	1502	C-Me	N(Me)propargyl	2-Cl-4-OMe-6-MePh
	1503	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Cl-4-OMe-6-MePh
	1504	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Cl-4-OMe-6-MePh
	1505	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Cl-4-OMe-6-MePh
	1506	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Cl-4-OMe-6-MePh
10	1507	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Cl-4-OMe-6-MePh
	1508	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ c-Pr	2-Cl-4-OMe-6-MePh
	1509	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Cl-4-OMe-6-MePh
	1510	C-Me	NHCH(c-Pr) ₂	2-Cl-4-OMe-6-MePh
	1511	C-Me	NHCH(Et) ₂	2-Cl-4-OMe-6-MePh
15	1512	C-Me	N(Et) ₂	2-Cl-4-OMe-6-MePh
	1513	C-Me	NEt(Bu)	2-Cl-4-OMe-6-MePh
	1514	C-Me	2-ethylpiperidyl	6-Me ₂ N-4-Me- pyrid-3-yl
20	1515	C-Me	cyclobutylamino	6-Me ₂ N-4-Me- pyrid-3-yl
	1516	C-Me	N(Me)CH ₂ CH=CH ₂	6-Me ₂ N-4-Me- pyrid-3-yl
	1517	C-Me	N(Et)CH ₂ c-Pr	6-Me ₂ N-4-Me- pyrid-3-yl
25	1518	C-Me	N(Pr)CH ₂ C-Pr	6-Me ₂ N-4-Me- pyrid-3-yl
	1519	C-Me	N(Me)Pr	6-Me ₂ N-4-Me- pyrid-3-yl
	1520	C-Me	N(Me)Et	6-Me ₂ N-4-Me- pyrid-3-yl
30	1521	C-Me	N(Me)Bu	6-Me ₂ N-4-Me- pyrid-3-yl
	1522	C-Me	N(Me)propargyl	6-Me ₂ N-4-Me- pyrid-3-yl
35	1523	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	6-Me ₂ N-4-Me-

				pyrid-3-yl
1524	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	6-Me ₂ N-4-Me-	
			pyrid-3-yl	
1525	C-Me	N (CH ₂ CH ₂ OMe) Me	6-Me ₂ N-4-Me-	
5			pyrid-3-yl	
1526	C-Me	N (CH ₂ CH ₂ OMe) Et	6-Me ₂ N-4-Me-	
			pyrid-3-yl	
1527	C-Me	N (CH ₂ CH ₂ OMe) Pr	6-Me ₂ N-4-Me-	
			pyrid-3-yl	
10	1528	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	6-Me ₂ N-4-Me-
			pyrid-3-yl	
	1529	C-Me	NH (CH (CH ₃) CH ₂ CH ₃)	6-Me ₂ N-4-Me-
			pyrid-3-yl	
15	1530	C-Me	NHCH (c-Pr) ₂	6-Me ₂ N-4-Me-
			pyrid-3-yl	
	1531	C-Me	N (CH ₂ CH ₂ OMe) ₂	6-Me ₂ N-4-Me-
			pyrid-3-yl	
	1532	C-Me	NHCH (Et) ₂	6-Me ₂ N-4-Me-
			pyrid-3-yl	
20	1533	C-Me	N (Et) ₂	6-Me ₂ N-4-Me-
			pyrid-3-yl	
	1534	C-Me	2-ethylpiperidyl	6-MeO-4-Me-
			pyrid-3-yl	
	1535	C-Me	cyclobutylamino	6-MeO-4-Me-
25			pyrid-3-yl	
	1536	C-Me	N (Me) CH ₂ CH=CH ₂	6-MeO-4-Me-
			pyrid-3-yl	
	1537	C-Me	N (Et) CH ₂ C-Pr	6-MeO-4-Me-
			pyrid-3-yl	
30	1538	C-Me	N (Pr) CH ₂ C-Pr	6-MeO-4-Me-
			pyrid-3-yl	
	1539	C-Me	N (Me) Pr	6-MeO-4-Me-
			pyrid-3-yl	
	1540	C-Me	N (Me) Et	6-MeO-4-Me-
35			pyrid-3-yl	
	1541	C-Me	N (Me) Bu	6-MeO-4-Me-

				pyrid-3-yl
1542	C-Me	N(Me) propargyl	6-MeO-4-Me-	pyrid-3-yl
1543	C-Me	NH (CH (CH ₃) CH (CH ₃) CH ₃)	6-MeO-4-Me-	pyrid-3-yl
5			6-MeO-4-Me-	pyrid-3-yl
1544	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	6-MeO-4-Me-	pyrid-3-yl
1545	C-Me	N (CH ₂ CH ₂ OMe) Me	6-MeO-4-Me-	pyrid-3-yl
10	1546	N (CH ₂ CH ₂ OMe) Et	6-MeO-4-Me-	pyrid-3-yl
	1547	N (CH ₂ CH ₂ OMe) Pr	6-MeO-4-Me-	pyrid-3-yl
15	1548	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	6-MeO-4-Me-	pyrid-3-yl
	1549	NH (CH (CH ₃) CH ₂ CH ₃)	6-MeO-4-Me-	pyrid-3-yl
	1550	NHCH (c-Pr) ₂	6-MeO-4-Me-	pyrid-3-yl
20	1551	N (CH ₂ CH ₂ OMe) ₂	6-MeO-4-Me-	pyrid-3-yl
	1552	NHCH (Et) ₂	6-MeO-4-Me-	pyrid-3-yl
	1553	N (Et) ₂	6-MeO-4-Me-	pyrid-3-yl
25	1554	2-ethylpiperidyl	4,6-Me ₂ -	pyrid-3-yl
	1555	cyclobutylamino	4,6-Me ₂ -	pyrid-3-yl
30	1556	N(Me) CH ₂ CH=CH ₂	4,6-Me ₂ -	pyrid-3-yl
	1557	N(Et) CH ₂ C-Pr	4,6-Me ₂ -	pyrid-3-yl
	1558	N(Pr) CH ₂ C-Pr	4,6-Me ₂ -	pyrid-3-yl
35	1559	N(Me) Pr	4,6-Me ₂ -	pyrid-3-yl

				pyrid-3-yl
1560	C-Me	N(Me) Et		4,6-Me ₂ -
1561	C-Me	N(Me) Bu		pyrid-3-yl 4,6-Me ₂ -
5				pyrid-3-yl 4,6-Me ₂ -
1562	C-Me	N(Me) propargyl		pyrid-3-yl 4,6-Me ₂ -
1563	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)		pyrid-3-yl 4,6-Me ₂ -
10	1564	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	pyrid-3-yl 4,6-Me ₂ -
	1565	C-Me	N(CH ₂ CH ₂ OMe)Me	pyrid-3-yl 4,6-Me ₂ -
	1566	C-Me	N(CH ₂ CH ₂ OMe)Et	pyrid-3-yl 4,6-Me ₂ -
15	1567	C-Me	N(CH ₂ CH ₂ OMe)Pr	pyrid-3-yl 4,6-Me ₂ -
	1568	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	pyrid-3-yl 4,6-Me ₂ -
20	1569	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	pyrid-3-yl 4,6-Me ₂ -
	1570	C-Me	NHCH(c-Pr) ₂	pyrid-3-yl 4,6-Me ₂ -
	1571	C-Me	N(CH ₂ CH ₂ OMe) ₂	pyrid-3-yl 4,6-Me ₂ -
25	1572	C-Me	NHCH(Et) ₂	pyrid-3-yl 4,6-Me ₂ -
	1573	C-Me	N(Et) ₂	pyrid-3-yl 4,6-Me ₂ -
30	1574	C-Me	2-ethylpiperidyl	pyrid-3-yl 2,6-Me ₂ -
	1575	C-Me	cyclobutylamino	pyrid-3-yl 2,6-Me ₂ -
	1576	C-Me	N(Me)CH ₂ CH=CH ₂	pyrid-3-yl 2,6-Me ₂ -
35	1577	C-Me	N(Et)CH ₂ C-Pr	pyrid-3-yl 2,6-Me ₂ -

			pyrid-3-yl
1578	C-Me	N(Pr)CH ₂ C-Pr	2,6-Me ₂ -
1579	C-Me	N(Me)Pr	pyrid-3-yl 2,6-Me ₂ -
5	1580	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1581	C-Me	pyrid-3-yl 2,6-Me ₂ -
10	1582	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1583	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1584	C-Me	pyrid-3-yl 2,6-Me ₂ -
15	1585	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1586	C-Me	pyrid-3-yl 2,6-Me ₂ -
20	1587	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1588	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1589	C-Me	pyrid-3-yl 2,6-Me ₂ -
25	1590	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1591	C-Me	pyrid-3-yl 2,6-Me ₂ -
30	1592	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1593	C-Me	pyrid-3-yl 2,6-Me ₂ -
	1594	C-Me	4-MeO-6-Me-
35	1595	C-Me	pyrid-3-yl 4-MeO-6-Me-

				pyrid-3-yl
	1596	C-Me	N (Me) CH ₂ CH=CH ₂	4-MeO-6-Me-
	1597	C-Me	N (Et) CH ₂ C-Pr	pyrid-3-yl 4-MeO-6-Me-
5	1598	C-Me	N (Pr) CH ₂ C-Pr	pyrid-3-yl 4-MeO-6-Me-
	1599	C-Me	N (Me) Pr	pyrid-3-yl 4-MeO-6-Me-
10	1600	C-Me	N (Me) Et	pyrid-3-yl 4-MeO-6-Me-
	1601	C-Me	N (Me) Bu	4-MeO-6-Me-
	1602	C-Me	N (Me) propargyl	pyrid-3-yl 4-MeO-6-Me-
15	1603	C-Me	NH (CH (CH ₃) CH (CH ₃) CH ₃)	pyrid-3-yl 4-MeO-6-Me-
	1604	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ CH=CH ₂	pyrid-3-yl 4-MeO-6-Me-
20	1605	C-Me	N (CH ₂ CH ₂ OMe) Me	pyrid-3-yl 4-MeO-6-Me-
	1606	C-Me	N (CH ₂ CH ₂ OMe) Et	pyrid-3-yl 4-MeO-6-Me-
	1607	C-Me	N (CH ₂ CH ₂ OMe) Pr	pyrid-3-yl 4-MeO-6-Me-
25	1608	C-Me	N (CH ₂ CH ₂ OMe) CH ₂ C-Pr	pyrid-3-yl 4-MeO-6-Me-
	1609	C-Me	NH (CH (CH ₃) CH ₂ CH ₃)	pyrid-3-yl 4-MeO-6-Me-
30	1610	C-Me	NHCH (C-Pr) ₂	pyrid-3-yl 4-MeO-6-Me-
	1611	C-Me	N (CH ₂ CH ₂ OMe) ₂	pyrid-3-yl 4-MeO-6-Me-
	1612	C-Me	NHCH (Et) ₂	pyrid-3-yl 4-MeO-6-Me-
35	1613	C-Me	N (Et) ₂	pyrid-3-yl 4-MeO-6-Me-

			pyrid-3-yl	
1614	C-Me	2-ethylpiperidyl	2-Br-4,5-(OMe) ₂ Ph	
1615	C-Me	cyclobutylamino	2-Br-4,5-(OMe) ₂ Ph	
1616	C-Me	N(Me)CH ₂ CH=CH ₂	2-Br-4,5-(OMe) ₂ Ph	
5	1617	C-Me	N(Et)CH ₂ C-Pr	2-Br-4,5-(OMe) ₂ Ph
	1618	C-Me	N(Pr)CH ₂ C-Pr	2-Br-4,5-(OMe) ₂ Ph
	1619	C-Me	N(Me)Pr	2-Br-4,5-(OMe) ₂ Ph
	1620	C-Me	N(Me)Et	2-Br-4,5-(OMe) ₂ Ph
	1621	C-Me	N(Me)Bu	2-Br-4,5-(OMe) ₂ Ph
10	1622	C-Me	N(Me)propargyl	2-Br-4,5-(OMe) ₂ Ph
	1623	C-Me	NH(CH(CH ₃)CH(CH ₃)CH ₃)	2-Br-4,5-(OMe) ₂ Ph
	1624	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ CH=CH ₂	2-Br-4,5-(OMe) ₂ Ph
	1625	C-Me	N(CH ₂ CH ₂ OMe)Me	2-Br-4,5-(OMe) ₂ Ph
	1626	C-Me	N(CH ₂ CH ₂ OMe)Et	2-Br-4,5-(OMe) ₂ Ph
15	1627	C-Me	N(CH ₂ CH ₂ OMe)Pr	2-Br-4,5-(OMe) ₂ Ph
	1628	C-Me	N(CH ₂ CH ₂ OMe)CH ₂ C-Pr	2-Br-4,5-(OMe) ₂ Ph
	1629	C-Me	NH(CH(CH ₃)CH ₂ CH ₃)	2-Br-4,5-(OMe) ₂ Ph
	1630	C-Me	NHCH(c-Pr) ₂	2-Br-4,5-(OMe) ₂ Ph
	1631	C-Me	N(CH ₂ CH ₂ OMe) ₂	2-Br-4,5-(OMe) ₂ Ph
20	1632	C-Me	NHCH(Et) ₂	2-Br-4,5-(OMe) ₂ Ph
	1633	C-Me	N(Et) ₂	2-Br-4,5-(OMe) ₂ Ph
	1634	C-Me	N <i>Et</i> (Bu)	2-Br -4,5-(OMe) ₂ Ph

Notes for Table 7:

- 25 a) CI-MS: 330 (M + H)⁺;
 b) CI-MS: 338 (M + H)⁺;
 c) CI-MS: 338 (M + H)⁺;
 d) CI-MS: 400 (M + H)⁺;
 f) CI-MS: 326 (M + H)⁺;
- 30 g) CI-MS: 354 (M + H)⁺;
 h) CI-MS: 336 (M + H)⁺;
 i) CI-MS: 354 (M + H)⁺;
 j) CI-MS: 378 (M + H)⁺;
 k) CI-HRMS: Calcd 356.2087 (M + H)⁺, Found: 356.2071:
 m) CI-MS: 340 (M + H)⁺;
 n) CI-MS: 368 (M + H)⁺;

- o) CI-MS: 326 (M + H)⁺;
p) CI-MS: 368 (M + H)⁺;
q) CI-MS: 394 (M + H)⁺;
r) CI-HRMS: Calcd 380.2087 (M + H)⁺, Found: 380.2078;
5 s) CI-HRMS: Calcd 356.2008 (M + H)⁺, Found: 356.1997;
t) CI-HRMS: Calcd 416.2220 (M + H)⁺, Found: 416.2005;
u) CI-HRMS: Calcd 370.2243 (M + H)⁺, Found: 370.2246;
v) CI-HRMS: Calcd 380.2400 (M + H)⁺, Found: 384.2382;
w) CI-HRMS: Calcd 429.2376 (M + H)⁺, Found: 429.2358;
10 w) CI-HRMS: Calcd 397.2478 (M + H)⁺, Found: 397.2484;

Utility

15

CRF-R1 Receptor Binding Assay for the Evaluation of Biological Activity

The following is a description of the
20 isolation of cell membranes containing cloned human CRF-
R1 receptors for use in the standard binding assay as
well as a description of the assay itself.

Messenger RNA was isolated from human hippocampus.
The mRNA was reverse transcribed using oligo (dt) 12-18
25 and the coding region was amplified by PCR from start to
stop codons. The resulting PCR fragment was cloned into
the EcoRV site of pGEMV, from whence the insert was
reclaimed using XhoI + XbaI and cloned into the XhoI +
XbaI sites of vector pm3ar (which contains a CMV
30 promoter, the SV40 't' splice and early poly A signals,
an Epstein-Barr viral origin of replication, and a
hygromycin selectable marker). The resulting expression
vector, called phchCRFR was transfected in 293EBNA cells
and cells retaining the episome were selected in the
35 presence of 400 µM hygromycin. Cells surviving 4 weeks

of selection in hygromycin were pooled, adapted to growth in suspension and used to generate membranes for the binding assay described below. Individual aliquots containing approximately 1×10^8 of the suspended cells
5 were then centrifuged to form a pellet and frozen.

For the binding assay a frozen pellet described above containing 293EBNA cells transfected with hCRFR1 receptors is homogenized in 10 ml of ice cold tissue buffer (50 mM HEPES buffer pH 7.0, containing 10 mM
10 MgCl₂, 2 mM EGTA, 1 µg/ml aprotinin, 1 µg/ml leupeptin and 1 µg/ml pepstatin). The homogenate is centrifuged at 40,000 x g for 12 min and the resulting pellet rehomogenized in 10 ml of tissue buffer. After another
15 centrifugation at 40,000 x g for 12 min, the pellet is resuspended to a protein concentration of 360 µg/ml to be used in the assay.

Binding assays are performed in 96 well plates; each well having a 300 µl capacity. To each well is added 50 µl of test drug dilutions (final concentration
20 of drugs range from 10^{-10} - 10^{-5} M), 100 µl of ¹²⁵I-ovine-CRF (¹²⁵I-o-CRF) (final concentration 150 pM) and 150 µl of the cell homogenate described above. Plates are then allowed to incubate at room temperature for 2 hours before filtering the incubate over GF/F filters
25 (presoaked with 0.3% polyethyleneimine) using an appropriate cell harvester. Filters are rinsed 2 times with ice cold assay buffer before removing individual filters and assessing them for radioactivity on a gamma counter.

30 Curves of the inhibition of ¹²⁵I-o-CRF binding to cell membranes at various dilutions of test drug are analyzed by the iterative curve fitting program LIGAND [P.J. Munson and D. Rodbard, *Anal. Biochem.* 107:220
35 (1980)], which provides Ki values for inhibition which are then used to assess biological activity.

A compound is considered to be active if it has a K_i value of less than about 10000 nM for the inhibition of CRF.

5 Inhibition of CRF-Stimulated Adenylate Cyclase Activity

Inhibition of CRF-stimulated adenylate cyclase activity can be performed as described by G. Battaglia et al. *Synapse* 1:572 (1987). Briefly, assays are 10 carried out at 37° C for 10 min in 200 ml of buffer containing 100 mM Tris-HCl (pH 7.4 at 37° C), 10 mM MgCl₂, 0.4 mM EGTA, 0.1% BSA, 1 mM isobutylmethylxanthine (IBMX), 250 units/ml phosphocreatine kinase, 5 mM creatine phosphate, 100 15 mM guanosine 5'-triphosphate, 100 nM oCRF, antagonist peptides (concentration range 10⁻⁹ to 10⁻⁶M) and 0.8 mg original wet weight tissue (approximately 40-60 mg protein). Reactions are initiated by the addition of 1 mM ATP/[³²P]ATP (approximately 2-4 mCi/tube) and 20 terminated by the addition of 100 ml of 50 mM Tris-HCL, 45 mM ATP and 2% sodium dodecyl sulfate. In order to monitor the recovery of cAMP, 1 μ l of [³H]cAMP (approximately 40,000 dpm) is added to each tube prior to separation. The separation of [³²P]cAMP 25 from [³²P]ATP is performed by sequential elution over Dowex and alumina columns.

In vivo Biological Assay

The *in vivo* activity of the compounds of the 30 present invention can be assessed using any one of the biological assays available and accepted within the art. Illustrative of these tests include the Acoustic Startle Assay, the Stair Climbing Test, and the Chronic Administration Assay. These and other models 35 useful for the testing of compounds of the present

invention have been outlined in C.W. Berridge and A.J. Dunn *Brain Research Reviews* 15:71 (1990).

Compounds may be tested in any species of rodent or small mammal.

5

Compounds of this invention have utility in the treatment of imbalances associated with abnormal levels of corticotropin releasing factor in patients suffering from depression, affective disorders, and/or anxiety.

Compounds of this invention can be administered to treat these abnormalities by means that produce contact of the active agent with the agent's site of action in the body of a mammal. The compounds can be administered by any conventional means available for use in conjunction with pharmaceuticals either as individual therapeutic agent or in combination of therapeutic agents. They can be administered alone, but will generally be administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The dosage administered will vary depending on the use and known factors such as pharmacodynamic character of the particular agent, and its mode and route of administration; the recipient's age, weight, and health; nature and extent of symptoms; kind of concurrent treatment; frequency of treatment; and desired effect. For use in the treatment of said diseases or conditions, the compounds of this invention can be orally administered daily at a dosage of the active ingredient of 0.002 to 200 mg/kg of body weight. Ordinarily, a dose of 0.01 to 10 mg/kg in divided doses one to four times a day, or in sustained release formulation will be effective in obtaining the desired pharmacological effect.

Dosage forms (compositions) suitable for administration contain from about 1 mg to about 100 mg of active ingredient per unit. In these pharmaceutical compositions, the active ingredient will ordinarily be 5 present in an amount of about 0.5 to 95% by weight based on the total weight of the composition.

The active ingredient can be administered orally in solid dosage forms, such as capsules, tablets and powders; or in liquid forms such as elixirs, syrups, 10 and/or suspensions. The compounds of this invention can also be administered parenterally in sterile liquid dose formulations.

Gelatin capsules can be used to contain the active ingredient and a suitable carrier such as but 15 not limited to lactose, starch, magnesium stearate, steric acid, or cellulose derivatives. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of 20 medication over a period of time. Compressed tablets can be sugar-coated or film-coated to mask any unpleasant taste, or used to protect the active ingredients from the atmosphere, or to allow selective disintegration of the tablet in the gastrointestinal 25 tract.

Liquid dose forms for oral administration can contain coloring or flavoring agents to increase patient acceptance.

In general, water, pharmaceutically acceptable 30 oils, saline, aqueous dextrose (glucose), and related sugar solutions and glycols, such as propylene glycol or polyethylene glycol, are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt 35 of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing

agents, such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or in combination, are suitable stabilizing agents. Also used are citric acid and its salts, and EDTA. In addition, parenteral 5 solutions can contain preservatives such as benzalkonium chloride, methyl- or propyl-paraben, and chlorobutanol.

Suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences", A. Osol, a 10 standard reference in the field.

Useful pharmaceutical dosage-forms for administration of the compounds of this invention can be illustrated as follows:

15 Capsules

A large number of units capsules are prepared by filling standard two-piece hard gelatin capsules each with 100 mg of powdered active ingredient, 150 mg lactose, 50 mg cellulose, and 6 mg magnesium stearate.

20 Soft Gelatin Capsules

A mixture of active ingredient in a digestible oil such as soybean, cottonseed oil, or olive oil is prepared and injected by means of a positive 25 displacement was pumped into gelatin to form soft gelatin capsules containing 100 mg of the active ingredient. The capsules were washed and dried.

Tablets

30 A large number of tablets are prepared by conventional procedures so that the dosage unit was 100 mg active ingredient, 0.2 mg of colloidal silicon dioxide, 5 mg of magnesium stearate, 275 mg of microcrystalline cellulose, 11 mg of starch, and 98.8 35 mg lactose. Appropriate coatings may be applied to increase palatability or delayed adsorption.

The compounds of this invention may also be used as reagents or standards in the biochemical study of neurological function, dysfunction, and disease.

5

Although the present invention has been described and exemplified in terms of certain preferred embodiments, other embodiments will be apparent to those skilled in the art. The invention is, therefore, not limited to the particular embodiments described and exemplified, but is capable of modification or variation without departing from the spirit of the invention, the full scope of which is delineated by the appended claims.

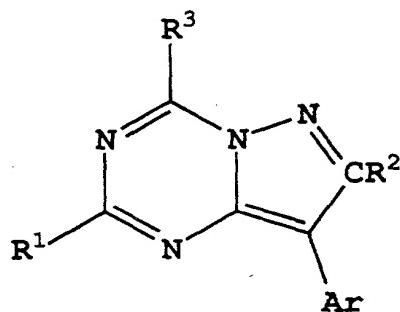
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CLAIMS

WHAT IS CLAIMED IS:

- 5 1. A method of treating affective disorder, anxiety, depression, headache, irritable bowel syndrome, post-traumatic stress disorder, supranuclear palsy, immune suppression, Alzheimer's disease, gastrointestinal diseases, anorexia nervosa or other
 10 feeding disorder, drug addiction, drug or alcohol withdrawal symptoms, inflammatory diseases, cardiovascular or heart-related diseases, fertility problems, human immunodeficiency virus infections, hemorrhagic stress, obesity, infertility, head and
 15 spinal cord traumas, epilepsy, stroke, ulcers, amyotrophic lateral sclerosis, hypoglycemia or a disorder the treatment of which can be effected or facilitated by antagonizing CRF, including but not limited to disorders induced or facilitated by CRF, in
 20 mammals comprising administering to the mammal a therapeutically effective amount of a compound of Formula (1):



(1)

25

and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and

pharmaceutically acceptable salt forms thereof,
wherein:

- Ar is selected from phenyl, naphthyl, pyridyl,
5 pyrimidinyl, triazinyl, furanyl, thienyl,
benzothienyl, benzofuranyl, 2,3-
dihydrobenzofuranyl, 2,3-dihydrobenzothienyl,
indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-
benzopyranyl, tetralinyl, each Ar optionally
10 substituted with 1 to 5 R⁴ groups and each Ar is
attached to an unsaturated carbon atom;
- R¹ is independently selected at each occurrence from
H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl,
15 halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl,
C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆
cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-
C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;
- 20 R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-
C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀
cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -
NR⁶R⁷, NR⁹COR¹⁰, -NR⁶S(O)_nR⁷, S(O)_nNR⁶R⁷, C₁-
C₄ haloalkyl, -OR⁷, SH or -S(O)_nR¹²;
- 25 R³ is selected from NR^{6a}R^{7a} and OR⁷;
- R⁴ is independently selected at each occurrence from:
C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl,
30 C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, NO₂,
halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, NR⁸COR⁷,
NR⁸CO₂R⁷, COR⁷, OR⁷, CONR⁶R⁷, CO(NOR⁹)R⁷, CO₂R⁷,
or S(O)_nR⁷, where each such C₁-C₁₀ alkyl, C₂-
C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl
35 and C₄-C₁₂ cycloalkylalkyl are optionally
substituted with 1 to 3 substituents

independently selected at each occurrence from C₁-C₄ alkyl, NO₂, halo, CN, NR⁶R⁷, NR⁸COR⁷, NR⁸CO₂R⁷, COR⁷ OR⁷, CONR⁶R⁷, CO₂R⁷, CO(NOR⁹)R⁷, or S(O)_nR⁷;

5

R⁶, R⁷, R^{6a} and R^{7a} are independently selected at each occurrence from:

-H,

-C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,

10

C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each optionally substituted with 1 to 3

15

substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵,

20

NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl, -aryl, aryl(C₁-C₄ alkyl), heteroaryl, heteroaryl(C₁-C₄ alkyl), heterocyclyl or heterocyclyl(C₁-C₄ alkyl);

25

alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each optionally substituted with 1-3 C₁-C₄ alkyl groups;

30

R⁸ is independently selected at each occurrence from H or C₁-C₄ alkyl;

35

R⁹ and R¹⁰ are independently selected at each occurrence from H, C₁-C₄ alkyl, or C₃-C₆ cycloalkyl;

R¹¹ is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl,
or C₃-C₆ cycloalkyl;

5 R¹² is C₁-C₄ alkyl or C₁-C₄ haloalkyl;

R¹³ is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-
C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-,
10 heteroaryl or heteroaryl(C₁-C₄ alkyl)-;

R¹⁵ and R¹⁶ are independently selected at each
occurrence from H, C₁-C₆ alkyl, C₃-C₁₀
cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that
15 for S(O)_nR¹⁵, R¹⁵ cannot be H;

aryl is phenyl or naphthyl, each optionally
substituted with 1 to 5 substituents
independently selected at
20 each occurrence from C₁-C₆ alkyl, C₃-
C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano,
OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵,
NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵,
NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

25 heteroaryl is pyridyl, pyrimidinyl, triazinyl,
furanyl, pyranyl, quinolinyl, isoquinolinyl,
thienyl, imidazolyl, thiazolyl, indolyl,
pyrrolyl, oxazolyl, benzofuranyl, benzothienyl,
30 benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-
dihydrobenzothienyl or 2,3-dihydrobenzofuranyl,
each being optionally substituted with 1 to 5
substituents independently selected at each
occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
35 halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH,
S(O)_nR¹⁵, -COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵,

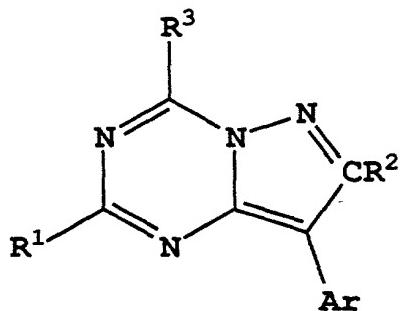
N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

heterocyclyl is saturated or partially saturated

- 5 heteroaryl, optionally substituted with 1 to 5
 substituents independently selected at each
 occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl,
 halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH,
 S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵,
10 N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and
 CONR¹⁶R¹⁵;

n is independently at each occurrence 0, 1 or 2.

- 15 2. A method of claim 1 wherein, in the compound of
 Formula (1), Ar is phenyl, pyridyl or 2,3-
 dihydrobenzofuranyl, each optionally substituted with
 1 to 4 R⁴ substituents.
- 20 3. A method of claim 1 wherein, in the compound of
 Formula (1), Ar is 2,4-dichlorophenyl, 2,4-
 dimethylphenyl or 2,4,6-trimethylphenyl, R¹ and R² are
 CH₃, and R³ is NR^{6a}R^{7a}.
- 25 4. A compound of Formula (1):



and isomers thereof, stereoisomeric forms thereof, or
 5 mixtures of stereoisomeric forms thereof, and
 pharmaceutically acceptable salt forms thereof
 wherein:

Ar is selected from phenyl, naphthyl, pyridyl,
 10 pyrimidinyl, triazinyl, furanyl, thienyl,
 benzothienyl, benzofuranyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl,
 indanyl, 1,2-benzopyranyl, 3,4-dihydro-1,2-benzopyranyl, tetralinyl, each Ar optionally
 15 substituted with 1 to 5 R⁴ groups and each Ar is
 attached to an unsaturated carbon atom;

R¹ is independently selected at each occurrence from
 H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl,
 20 halo, CN, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl,
 C₂-C₁₂ alkoxyalkyl, C₂-C₁₀ cyanoalkyl, C₃-C₆
 cycloalkyl, C₄-C₁₀ cycloalkylalkyl, NR⁹R¹⁰, C₁-C₄ alkyl-NR⁹R¹⁰, NR⁹COR¹⁰, OR¹¹, SH or S(O)_nR¹²;

25 R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -

NR^6R^7 , $\text{NR}^9\text{COR}^{10}$, $-\text{NR}^6\text{S(O)}_n\text{R}^7$, $\text{S(O)}_n\text{NR}^6\text{R}^7$, $\text{C}_1\text{-C}_4$ haloalkyl, $-\text{OR}^7$, SH or $-\text{S(O)}_n\text{R}^{12}$;

R^3 is selected from $\text{NR}^6\text{aR}^7\text{a}$ and OR^7 ;

5

R^4 is independently selected at each occurrence from:

$\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl,

$\text{C}_3\text{-C}_6$ cycloalkyl, $\text{C}_4\text{-C}_{12}$ cycloalkylalkyl, NO_2 ,

halo, CN, $\text{C}_1\text{-C}_4$ haloalkyl, NR^6R^7 , NR^8COR^7 ,

10 $\text{NR}^8\text{CO}_2\text{R}^7$, COR^7 , OR^7 , CONR^6R^7 , $\text{CO(NOR}^9\text{)R}^7$, CO_2R^7 ,
or $\text{S(O)}_n\text{R}^7$, where each such $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_2\text{-C}_{10}$ alkynyl, $\text{C}_3\text{-C}_6$ cycloalkyl and $\text{C}_4\text{-C}_{12}$ cycloalkylalkyl are optionally substituted with 1 to 3 substituents

15

independently selected at each occurrence from

$\text{C}_1\text{-C}_4$ alkyl, NO_2 , halo, CN, NR^6R^7 , NR^8COR^7 ,

$\text{NR}^8\text{CO}_2\text{R}^7$, COR^7 OR^7 , CONR^6R^7 , CO_2R^7 , $\text{CO(NOR}^9\text{)R}^7$,

or $\text{S(O)}_n\text{R}^7$;

20 R^6 , R^7 , R^6a and R^7a are independently selected at each occurrence from:

-H,

$-\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_3\text{-C}_{10}$ alkenyl, $\text{C}_3\text{-C}_{10}$ alkynyl,

$\text{C}_1\text{-C}_{10}$ haloalkyl with 1-10 halogens, $\text{C}_2\text{-C}_8$

25

alkoxyalkyl, $\text{C}_3\text{-C}_6$ cycloalkyl, $\text{C}_4\text{-C}_{12}$ cycloalkylalkyl, $\text{C}_5\text{-C}_{10}$ cycloalkenyl,

or $\text{C}_6\text{-C}_{14}$ cycloalkenylalkyl, each

optionally substituted with 1 to 3

substituents independently selected at each occurrence from $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_6$ cycloalkyl, halo, $\text{C}_1\text{-C}_4$ haloalkyl,

cyan, OR^{15} , SH, $\text{S(O)}_n\text{R}^{13}$, COR^{15} , CO_2R^{15} ,

OC(O)R^{13} , $\text{NR}^8\text{COR}^{15}$, $\text{N}(\text{COR}^{15})_2$, $\text{NR}^8\text{CONR}^{16}\text{R}^{15}$,

$\text{NR}^8\text{CO}_2\text{R}^{13}$, $\text{NR}^{16}\text{R}^{15}$, $\text{CONR}^{16}\text{R}^{15}$, aryl,

30

heteroaryl or heterocyclyl.

35

-aryl, aryl(C₁-C₄ alkyl), heteroaryl,
heteroaryl(C₁-C₄ alkyl), heterocyclyl or
heterocyclyl(C₁-C₄ alkyl),
alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently
5 piperidine, pyrrolidine, piperazine, N-
methylpiperazine, morpholine or thiomorpholine, each
optionally substituted with 1-3 C₁-C₄ alkyl groups;

10 R⁸ is independently selected at each occurrence from H
or C₁-C₄ alkyl;

15 R⁹ and R¹⁰ are independently selected at each
occurrence from H, C₁-C₄ alkyl, or C₃-C₆
cycloalkyl;

20 R¹¹ is selected from H, C₁-C₄ alkyl, C₁-C₄ haloalkyl,
or C₃-C₆ cycloalkyl;

25 R¹² is C₁-C₄ alkyl or C₁-C₄ haloalkyl;

30 R¹³ is selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-
C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-
C₁₂ cycloalkylalkyl, aryl, aryl(C₁-C₄ alkyl)-,
heteroaryl or heteroaryl(C₁-C₄ alkyl)-;

35 R¹⁵ and R¹⁶ are independently selected at each
occurrence from H, C₁-C₆ alkyl, C₃-C₁₀
cycloalkyl, C₄-C₁₆ cycloalkylalkyl, except that
for S(O)_nR¹⁵, R¹⁵ cannot be H;

aryl is phenyl or naphthyl, each optionally
substituted with 1 to 5 substituents
independently selected at
each occurrence from C₁-C₆ alkyl, C₃-
C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano,

OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

5 heteroaryl is pyridyl, pyrimidinyl, triazinyl, furanyl, pyranyl, quinolinyl, isoquinolinyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrrolyl, oxazolyl, benzofuranyl, benzothienyl, benzothiazolyl, isoxazolyl, pyrazolyl, 2,3-dihydrobenzothienyl or 2,3-dihydrobenzofuranyl,
10 each being optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, -COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵,
15 N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁶R¹⁵, and CONR¹⁶R¹⁵;

20 heterocyclyl is saturated or partially saturated heteroaryl, optionally substituted with 1 to 5 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹⁵, COR¹⁵, CO₂R¹⁵, OC(O)R¹⁵, NR⁸COR¹⁵,
25 N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹⁵, NR¹⁵R¹⁶, and CONR¹⁶R¹⁵;

n is independently at each occurrence 0, 1 or 2;

30 with the provisos that:

(1) when R² is H and R³ is -OR⁷ and R⁷ is H, then R¹ is not H, OH or SH;

- (2) when R^1 is CH_3 or C_2H_5 and R^2 is H, and R^3 is OH, NHC_4H_9 , or $N(C_2H_5)_2$, then Ar is not phenyl or m- CH_3 -phenyl,
- 5 (3) when R^2 is H and Ar is pyridyl, pyrimidinyl or pyrazinyl, and R^3 is $NR^{6a}R^{7a}$, then R^{6a} and R^{7a} are not H or alkyl;
- 10 (4) when R^2 is $SO_2NR^6R^7$, then R^3 is not OH; and
- 10 (5) when R^2 is $-NR^6SO_2R^7$ or $-SO_2NR^6R^7$, then R^3 is not OH.
- 15 5. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof with the additional provisos that: (1) when R^1 is H, C_1-C_4 alkyl, halo, CN, C_1-C_{12} hydroxyalkyl, C_1-C_4 alkoxyalkyl or $SO_2(C_1-C_4$ alkyl) and R^3 is $NR^{6a}R^{7a}$ and R^{6a} is unsubstituted C_1-C_4 alkyl, then R^{7a} is not phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, indolyl or C_3-C_6 cycloalkyl; and (2) when R^1 is H, C_1-C_4 alkyl, halo, CN, C_1-C_{12} hydroxyalkyl, C_1-C_4 alkoxyalkyl or $SO_2(C_1-C_4$ alkyl) and R^3 is $NR^{6a}R^{7a}$ and R^{7a} is unsubstituted C_1-C_4 alkyl, then R^{6a} is not phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, furanyl, benzofuranyl, benzothiazolyl, indolyl or C_3-C_6 cycloalkyl.
- 30 6. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein: Ar is phenyl,

pyridyl or 2,3-dihydrobenzofuranyl, each optionally substituted with 1 to 4 R⁴ substituents.

7. A compound of claim 6 and isomers thereof,
5 stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein: Ar is 2,4-dichlorophenyl, 2,4-dimethylphenyl or 2,4,6-trimethylphenyl, and R¹ and R² are CH₃.
- 10 8. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 4.
- 15 9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 6.
- 20 10. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 7.
- 25 11. A compound of claim 6 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:
- R^{6a} is independently selected from:
30 -H,
-C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl, C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each
35 optionally substituted with 1 to 3 substituents independently selected at each

- occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl, -aryl, aryl(C₁-C₄ alkyl)-, heteroaryl, heteroaryl(C₁-C₄ alkyl)-, heterocyclyl or heterocyclyl(C₁-C₄ alkyl)-; and
- 10 R^{7a} is independently selected at each occurrence from:
 -H,
 -C₅-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
 C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl, or C₆-C₁₄ cycloalkenylalkyl, each
 15 optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl,
 20 -aryl, aryl(C₁-C₄ alkyl), heteroaryl, heteroaryl(C₁-C₄ alkyl), heterocyclyl or heterocyclyl(C₁-C₄ alkyl);
- 25 alternatively, NR⁶R⁷ and NR^{6a}R^{7a} are independently selected at each occurrence from:
 piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine or thiomorpholine, each
 30 optionally substituted with 1-3 C₁-C₄ alkyl groups.
12. A compound of claim 6 and isomers thereof,
 35 stereoisomeric forms thereof, or mixtures of

stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

- R^{6a} and R^{7a} are identical and are selected from:
- 5 -C₁-C₄ alkyl or C₃-C₆ cycloalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, -COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, 10 aryl, heteroaryl or heterocyclyl, and -aryl or heteroaryl.
- 15 13. A compound of claim 6 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:
- 20 R^{6a} is selected from:
-H,
-C₁-C₁₀ alkyl, C₃-C₁₀ alkenyl, C₃-C₁₀ alkynyl,
C₁-C₁₀ haloalkyl with 1-10 halogens, C₂-C₈ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-25 C₁₂ cycloalkylalkyl, C₅-C₁₀ cycloalkenyl,
or C₆-C₁₄ cycloalkenylalkyl, each optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, 30 aryl, heteroaryl or heterocyclyl,

-aryl, aryl(C₁-C₄ alkyl), heteroaryl,
heteroaryl(C₁-C₄ alkyl), heterocyclyl or
heterocyclyl(C₁-C₄ alkyl);

R^{7a} is selected from:

- 5 -C₁-C₄ alkyl and each such C₁-C₄ alkyl is
 substituted with 1-3 substituents
 independently selected at each occurrence from
 C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
 haloalkyl, cyano, OR¹⁵, SH, S(O)nR¹³, COR¹⁵,
10 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
 NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
 aryl, heteroaryl or heterocyclyl.

14. A compound of claim 6 and isomers thereof,
15 stereoisomeric forms thereof, or mixtures of
 stereoisomeric forms thereof, and pharmaceutically
 acceptable salt forms thereof wherein:

- one of R^{6a} and R^{7a} is selected from:
20 -C₃-C₆ cycloalkyl, each such C₃-C₆ cycloalkyl
 optionally substituted with 1-3 substituents
 independently selected at each occurrence from
 C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
 haloalkyl, cyano, OR¹⁵, SH, S(O)nR¹³, COR¹⁵,
25 CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
 NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
 aryl, heteroaryl or heterocyclyl,
 -aryl,
 -heteroaryl or
30 -heterocyclyl,
and the other of R^{6a} and R^{7a} is unsubstituted C₁-C₄
 alkyl.

15. A compound of claim 6 and isomers thereof,
35 stereoisomeric forms thereof, or mixtures of

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- stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl, each such C₁-C₁₀ alkyl optionally substituted with
- 5 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl,
- 10 heteroaryl or heterocyclyl.
16. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:
- 15 -Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents;
- R¹ and R² are independently selected from H, C₁-C₄
- 20 alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.
17. A compound of claim 11 and isomers thereof, stereoisomeric forms thereof, or mixtures of
- 25 stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:
- Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl, and each Ar is optionally substituted with 1 to 4 R⁴ substituents;
- R¹ and R² are independently selected from H, C₁-C₄
- 30 alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.
18. A compound of claim 12 and isomers thereof,
- 35 stereoisomeric forms thereof, or mixtures of

stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

-Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents;

5 -R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

10 19. A compound of claim 13 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

15 -Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents;
-R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

20 20. A compound of claim 14 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

25 -Ar is phenyl, pyridyl or 2,3-dihydrobenzofuranyl,
and each Ar is optionally substituted with 1
to 4 R⁴ substituents;
-R¹ and R² are independently selected from H, C₁-C₄ alkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

30 21. A compound of claim 16 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein:

one of R^{6a} and R^{7a} is selected from:

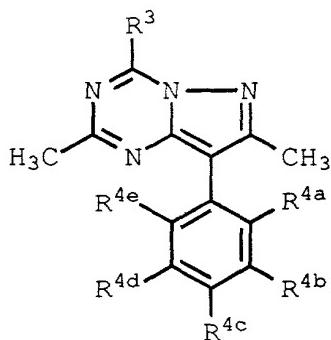
-C₃-C₆ cycloalkyl, each such C₃-C₆ cycloalkyl
optionally substituted with 1-3 substituents
independently selected at each occurrence from
C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄
haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵,
CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂,
NR⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵,
aryl, heteroaryl or heterocyclyl,
-aryl,
-heteroaryl or
-heterocyclyl,

and the other of R^{6a} and R^{7a} is unsubstituted C₁-C₄ alkyl.

- 15 22. A compound of claim 16 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein
- 20 R^{6a} and R^{7a} are independently H or C₁-C₁₀ alkyl, each such C₁-C₁₀ alkyl optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₆ alkyl, C₃-C₆ cycloalkyl, halo, C₁-C₄ haloalkyl, cyano, OR¹⁵, SH, S(O)_nR¹³, COR¹⁵, CO₂R¹⁵, OC(O)R¹³, NR⁸COR¹⁵, N(COR¹⁵)₂, R⁸CONR¹⁶R¹⁵, NR⁸CO₂R¹³, NR¹⁶R¹⁵, CONR¹⁶R¹⁵, aryl, heteroaryl or heterocyclyl.

- 25 23. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R¹ is independently selected at each occurrence from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₁-C₄ haloalkyl, C₁-C₁₂ hydroxyalkyl, C₂-C₁₂ alkoxyalkyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl.

24. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R² is selected from H, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₂-C₄ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, C₁-C₄ hydroxyalkyl, halo, CN, -NR⁶R⁷, C₁-C₄ haloalkyl, -OR⁷.
- 5 10 25. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R⁴ is independently selected at each occurrence from: H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₆ cycloalkyl, C₄-C₁₂ cycloalkylalkyl, halo, CN, C₁-C₄ haloalkyl, NR⁶R⁷, COR⁷, OR⁷, S(O)_n(C₁-C₁₀ alkyl), where each such C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₆ cycloalkyl and C₄-C₁₂ cycloalkylalkyl are 20 optionally substituted with 1 to 3 substituents independently selected at each occurrence from C₁-C₄ alkyl, NR⁶R⁷, COR⁷ OR⁷, CO₂R⁷ and where R⁷ in SONR⁷ is C₁-C₁₀ alkyl.
- 15 25 26. A compound of claim 4 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof wherein R⁴ is independently selected at each occurrence from: H, C₁-C₁₀ alkyl, C₁-C₄ alkoxy, halo, CN and -NR⁶R⁷.
- 30 27. A compound of Formula (50)



FORMULA (50)

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- 5 and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof, selected from the group consisting of:
- 10 a compound of Formula (50) wherein R³ is -NHCH(n-Pr)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -NHCH(Et)(n-Bu), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -NHCH(CH₂OEt)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -N(Me)(Ph), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -NHCH(Et)(n-Pr), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -
- 25 NHCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -OEt, R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -N(CH₂CN)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(Me)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -OCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(n-Pr)(CH₂cPr), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NHCH(Me)(CH₂N(Me)₂), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(cPr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(n-Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -N(n-Bu)(CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is -NHCH(Et)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;

a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is -
 NHCH(Et)(CH₂OMe), R^{4a} is Br, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is
 Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is Me;
- 10 a compound of Formula (50) wherein R³ is -NHCH(CH₂OEt)₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is
 Me;
- 15 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂CH₂OMe)(CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 is Me, R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R³ is morpholino, R^{4a}
 is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
 R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 30 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -NH(c-Pr), R^{4a}
 is Me, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂,
 R^{4a} is CN, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- a compound of Formula (50) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Me, R^{4d}
 is H and R^{4e} is Me;
- a compound of Formula (50) wherein R³ is -NCH(CH₂OMe)₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is
 H;

- a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 is Br, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 10 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 15 a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is
 H;
- 20 a compound of Formula (50) wherein R³ is -
 NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is Me,
 R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c}
 is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d}
 is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -N(c-
 Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d}
 is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is (S)-
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c}
 is Cl, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c}
 is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -
 NH(CH₂OMe)(CH₂-iPr), R^{4a} is Me, R^{4b} is H, R^{4c} is
 10 Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is H, R^{4d} is H and R^{4e} is
 H;
- 15 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is NMe₂, R^{4d} is H and R^{4e}
 is H;
- 20 a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(n-Pr), R^{4a} is Me, R^{4b} is H, R^{4c} is Me,
 R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -
 25 NHCH(CH₂OEt)(Et), R^{4a} is Me, R^{4b} is H, R^{4c} is Me,
 R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -
 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
 30 is NMe₂, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is
 Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
 R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is
 40 H;

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- a compound of Formula (50) wherein R³ is -NHCH(CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is Br, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- 10 10 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
15 15 is Me, R^{4b} is H, R^{4c} is NMe₂, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is (S)-
20 20 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
is Me, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -
25 25 NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
is Me, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -
NHCH(CH₂OMe)(CH₂CH₂OMe), R^{4a} is Me, R^{4b} is H, R^{4c}
is Cl, R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(c-
35 35 Pr)(CH₂CH₂CN), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d}
is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -NH(Et)(CH₂CN),
40 40 R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is -
N(CH₂CH₂OMe)(CH₂CH₂OH), R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is -N(CH₂CH₂OMe)₂,
R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is Me, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is -N(c-Pr) (n-
Pr), R^{4a} is Me, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is -NHCH (Et)₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -
NHCH(Et)(CH₂OMe), R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- a compound of Formula (50) wherein R³ is -N(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is CN, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is -N(c-
Pr)(CH₂CH₂CN), R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(CH₂OH)₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is Cl, R^{4d} is H and R^{4e} is H; and

- a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

5 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

10 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

25 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

30 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- 5 a compound of Formula (50) wherein R³ is N(Et)propargyl,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

10 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is H and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
 H and R^{4e} is H;

20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
 1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
 and R^{4e} is H;

- a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

- a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is
 Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
 R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
 and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 35 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
 is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 40 a compound of Formula (50) wherein R³ is -NHCH(Et)₂, R^{4a}
 is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
 H;

a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- 5 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- 15 a compound of Formula (50) wherein R^3 is $N(Et)CH_2CH=CH_2$,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

- a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

- a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

- 25 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

- 30 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- 35 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(Me)propargyl,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;

- 5 a compound of Formula (50) wherein R³ is
 $\text{NHCH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}_3$, R^{4a} is OMe, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is H;

10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is
H and R^{4e} is H;

15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
and R^{4e} is H;

35 a compound of Formula (50) wherein R³ is
 $\text{NHCH}(\text{CH}_3)\text{CH}_2\text{CH}_3$, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;

40 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
H;

a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
H;

- a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;

- 0 9 0 1 3 0 0 0 2 - 0 1 2 8 9 6
- a compound of Formula (50) wherein R³ is N(Me)propargyl,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 5 a compound of Formula (50) wherein R³ is N(Et)propargyl,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 10 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is
 OMe, R^{4d} is Me and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂CH=CH₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is
 Me and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂cPr, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me
 and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH₂CH₃, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is Me and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
 is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is
 H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
 R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e}
 is H;

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- a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is OMe, R^{4b} is H, R^{4c} is OMe, R^{4d} is Me and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 25 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 30 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 40 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 40 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;

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- a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 5 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 10 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 15 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;
- 40 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;

- 5 a compound of Formula (50) wherein R^3 is $NHCH(cPr)_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is Me;

10 a compound of Formula (50) wherein R^3 is $NHCH(Et)_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

15 a compound of Formula (50) wherein R^3 is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

20 a compound of Formula (50) wherein R^3 is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

25 a compound of Formula (50) wherein R^3 is $N(Me)CH_2CH=CH_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

30 a compound of Formula (50) wherein R^3 is $N(Et)CH_2CH=CH_2$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

35 a compound of Formula (50) wherein R^3 is $N(Me)CH_2cPr$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

40 a compound of Formula (50) wherein R^3 is $N(Pr)CH_2cPr$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

a compound of Formula (50) wherein R^3 is $N(Me)Pr$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

a compound of Formula (50) wherein R^3 is $N(Me)Et$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

- a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

5 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

10 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

15 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

40 a compound of Formula (50) wherein R³ is NHCH(CH₃)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

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- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

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- a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 10 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 15 a compound of Formula (50) wherein R³ is N(Et)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;

- a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is OMe;
- 5 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
 is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
 OMe;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is OMe;
- 15 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
 is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is
 OMe;
- a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is
 Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is OMe;
- 20 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
 is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
 1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and
 R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is cyclobutyl-
 amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 35 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;

- a compound of Formula (50) wherein R³ is N(Et)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 5 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)Pr, R^{4a} is
Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is
Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is
Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Et)propargyl,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;
- 30 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is
OMe, R^{4d} is H and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is
H and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
is H;

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- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e}
 is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
 CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H
 and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is
 NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
 R^{4d} is H and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
 is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a}
 is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is H and R^{4e} is H.
- 30 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
 1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and
 R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is cyclobutyl-
 amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F
 and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂,
 R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
 is H;

- a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Me)cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 20 20 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 25 25 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH(CH₃)CH₃), R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 35 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 40 40

- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F
and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is
NH(CH(CH₃)CH₂CH₃), R^{4a} is Cl, R^{4b} is F, R^{4c} is OMe,
R^{4d} is H and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e}
is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H.
- 40 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
1-yl, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe
and R^{4e} is H;
- a compound of Formula (50) wherein R³ is cyclobutyl-
amino, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe
and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH(CH₃)CH₃), R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;

- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-
CH₂cPr, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe
and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is
NHCH(CH₃)CH₂CH₃, R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e}
is H;
- 35 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Cl, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is
H;
- 40 a compound of Formula (50) wherein R³ is 2-ethylpiperid-
1-yl, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe
and R^{4e} is H;

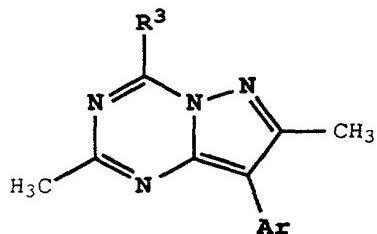
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- a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH(CH₃)CH₃, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

- CONFIDENTIAL
- a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is NH(CH(CH₃)CH₂CH₃), R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

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- a compound of Formula (50) wherein R³ is 2-ethylpiperid-1-yl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5
- a compound of Formula (50) wherein R³ is cyclobutyl-amino, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(Me)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(Et)CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(Me)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is N(Et)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is N(Pr)CH₂cPr, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(Me)Et, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- a compound of Formula (50) wherein R³ is N(Me)Bu, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is N(Me)propargyl, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;

- a compound of Formula (50) wherein R³ is
 $\text{NH}(\text{CH}(\text{CH}_3)\text{CH}(\text{CH}_3)\text{CH}_3$, R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 5 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is F and R^{4e} is H;
- 10 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Me,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 15 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Et,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 20 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)Pr,
R^{4a} is Br, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 25 a compound of Formula (50) wherein R³ is
 $\text{NH}(\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$, R^{4a} is Me, R^{4b} is H, R^{4c} is OMe,
R^{4d} is OMe and R^{4e} is H;
- 30 a compound of Formula (50) wherein R³ is NHCH(cPr)₂, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 35 a compound of Formula (50) wherein R³ is N(CH₂CH₂OMe)₂,
R^{4a} is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
- 40 a compound of Formula (50) wherein R³ is NHCH(Et)₂, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H;
a compound of Formula (50) wherein R³ is N(Et)₂, R^{4a}
is Me, R^{4b} is H, R^{4c} is OMe, R^{4d} is OMe and R^{4e} is H.

28. A compound of claim 4 of Formula (60)



FORMULA (60)

5

and isomers thereof, stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, and pharmaceutically acceptable salt forms thereof, selected from the group consisting of:

10

a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

15

a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

20

a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

25

a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is NH(CH(CH₃)CH₂CH₃), Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is NHCH(cPr)₂ Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(Et)CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Et, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)propargyl, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is NH(CH(CH₃)CH(CH₃)CH₃), Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is NH(CH(CH₃)CH₂CH₃), Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar is 6-dimethylamino-4-methylpyrid-3-yl.
- 25 a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 6-methoxy-4-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 6-methoxy-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 6-methoxy-4-methylpyrid-3-yl;
- 35 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar is 6-methoxy-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,

- Ar is 6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
6- methoxy -4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
6- methoxy -4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- 15 15 a compound of Formula (60) wherein R³ is N(Et)propargyl,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, Ar is 6- methoxy -4-
methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 6- methoxy -4-methylpyrid-3-yl;
- 25 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
Ar is 6- methoxy -4-methylpyrid-3-yl;
- 30 30 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
Ar is 6- methoxy -4-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, Ar is 6-methoxy-4-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is NHCH(CH₃)CH₂CH₃, Ar is 6-methoxy-4-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is NHCH(cPr)₂ Ar
is 6-methoxy-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 6-methoxy-4-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar is
6-methoxy-4-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
6-methoxy-4-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂,
Ar is 4-methoxy-6-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar
is 4-methoxy-6-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Et, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)propargyl, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 15 15 a compound of Formula (60) wherein R³ is NHCH(CH₃)CH(CH₃)CH₃, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂CH=CH₂, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 25 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et, Ar is 4-methoxy-6-methylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr, Ar is 4-methoxy-6-methylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is NH(CH(CH₃)CH₂CH₃), Ar is 4-methoxy-6-methylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar is 6-methoxy-4-methylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is 4-methoxy-6-methylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 4,6-dimethylpyrid-3-yl;
- 35 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 4,6-dimethylpyrid-3-yl;
- 40 a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar is 4,6-dimethylpyrid-3-yl;
- 45 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr,

- Ar is 4,6-dimethylpyrid-3-yl;
a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
4,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Et Ar is
4,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 4,6-dimethylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(Et)propargyl,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
NHCH(CH₃)CH(CH₃)CH₃, Ar is 4,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 4,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
Ar is 4,6-dimethylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
Ar is 4,6-dimethylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-CH₂cPr, Ar is 4,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is NHCH(CH₃)CH₂CH₃, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar is 4,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is NHCH(Et)₂ Ar is 4,6-dimethylpyrid-3-yl;
- 15 a compound of Formula (60) wherein R³ is N(Et)₂, Ar is 4,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is 2-ethylpiperid-1-yl, Ar is 2,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is cyclobutyl-amino, Ar is 2,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(Me)CH₂CH=CH₂, Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Et)CH₂cPr, Ar is Ar is 2,6-dimethylpyrid-3-yl;
- 30 a compound of Formula (60) wherein R³ is N(Pr)CH₂cPr, Ar is Ar is 2,6-dimethylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is N(Me)Pr, Ar is
2,6-dimethylpyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is N(Me)Et, Ar is
2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(Me)Bu, Ar is
2,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is N(Me)propargyl,
Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is
15 NH(CH(CH₃)CH(CH₃)CH₃), Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
CH₂CH=CH₂, Ar is 2,6-dimethylpyrid-3-yl;
- 20 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Me,
Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Et,
Ar is 2,6-dimethylpyrid-3-yl;
- 25 a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)Pr,
Ar is 2,6-dimethylpyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)-
30 CH₂cPr, Ar is 2,6-dimethylpyrid-3-yl;

- a compound of Formula (60) wherein R³ is
NH(CH(CH₃)CH₂CH₃), Ar is 2,6-dimethyl pyrid-3-yl;
- 5 a compound of Formula (60) wherein R³ is NHCH(cPr)₂, Ar
is 2,6-dimethyl pyrid-3-yl;
- a compound of Formula (60) wherein R³ is N(CH₂CH₂OMe)₂,
Ar is 2,6-dimethylpyrid-3-yl;
- 10 a compound of Formula (60) wherein R³ is NHCH(Et)₂, Ar
is 2,6-dimethyl-pyrid-3-yl; and
- a compound of Formula (60) wherein R³ is N(Et)₂, Ar is
2,6-dimethyl-pyrid-3-yl.
- 15 29. A compound of claim 4 and isomers thereof,
stereoisomeric forms thereof, or mixtures of
stereoisomeric forms thereof, and pharmaceutically
acceptable salt forms thereof, wherein said compound
20 is selected from the group consisting of:
- 4-((2-butyl)amino)-2,7-dimethyl-8-(2-methyl-4-
methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 25 4-((2-butyl)amino)-2,7-dimethyl-8-(2,5-di methyl-4-
methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 4-((3-pentyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-
methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 30 4-((3-pentyl)amino)-2,7-dimethyl-8-(2-methyl-4-
methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;

- 4-(N-cyclopropylmethyl-N-propylamino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 5 4-(N-cyclopropylmethyl-N-propylamino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 10 4-(N-allyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 15 4-(N-allyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 20 4-(diallylamino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine;
- 25 4-(N-ethyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2-methyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine; and
- 30 4-(N-ethyl-N-(2-methoxyethyl)amino)-2,7-dimethyl-8-(2,5-dimethyl-4-methoxyphenyl)-[1,5-a]-pyrazolo-1,3,5-triazine.
- 35 30. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claims 6, 11, 16, 27, 28 and 29.

31. A method of treating affective disorder, anxiety,
depression, headache, irritable bowel syndrome, post-
traumatic stress disorder, supranuclear palsy, immune
suppression, Alzheimer's disease, gastrointestinal
diseases, anorexia nervosa or other feeding disorder,
drug addiction, drug or alcohol withdrawal symptoms,
inflammatory diseases, cardiovascular or heart-related
diseases, fertility problems, human immunodeficiency
virus infections, hemorrhagic stress, obesity,
infertility, head and spinal cord traumas, epilepsy,
stroke, ulcers, amyotrophic lateral sclerosis,
hypoglycemia or a disorder the treatment of which can be
effected or facilitated by antagonizing CRF, including
but not limited to disorders induced or facilitated by
CRF, in mammals comprising administering to the mammal a
therapeutically effective amount of a compound of claim
claims 4, 6, 11, 16, 27, 28 and 29.

20

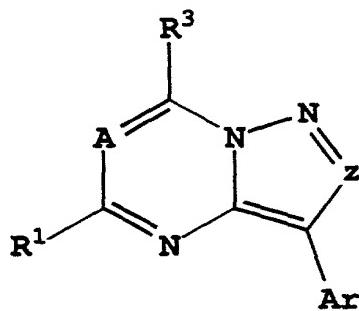
TITLE

AZOLO TRIAZINES AND PYRIMIDINES

5

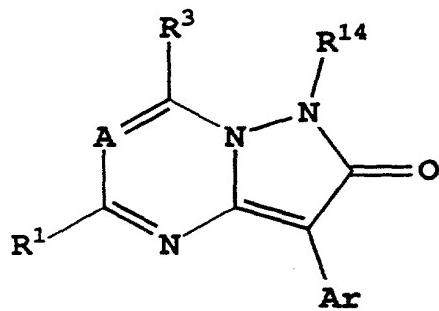
ABSTRACT OF THE DISCLOSURE

Corticotropin releasing factor (CRF) antagonists of formula I or II:



10

(I)



(II)

and their use in treating anxiety, depression, and other psychiatric, neurological disorders as well as treatment of immunological, cardiovascular or heart-related diseases and colonic hypersensitivity associated with psychopathological disturbance and stress.

DECLARATION and POWER OF ATTORNEY

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

the specification of which is attached hereto unless the following box is checked:

was filed on _____ as U.S. Application No. _____ or PCT International Application No. _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is known to me to be material to patentability as defined in 37 CFR § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed.

Application No.	Country	Filing Date	Priority Claimed (Yes/No)
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I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States Provisional Application(s) listed below.

U.S. Provisional Application No.	U.S. Filing Date
60/023,290	7/24/96

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s), or § 365(c) of any PCT International Application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application or PCT International Application in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information which is known to me to be material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

Application No.	U.S. Filing Date	Status (patented, pending or abandoned)
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POWER OF ATTORNEY: I hereby appoint the following attorney(s) and/or agent(s) the power to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

Name:	Blair Q. Ferguson Gerald J. Boudreaux Norbert Reinert Karen H. Kondrad David H. Vance (Agent) Scott K. Larsen (Agent) Robert W. Black Maureen P. O'Brien	Registration No.: 34,329 35,073 18,926 38,212 38,644 38,532 19,688 P-42,043
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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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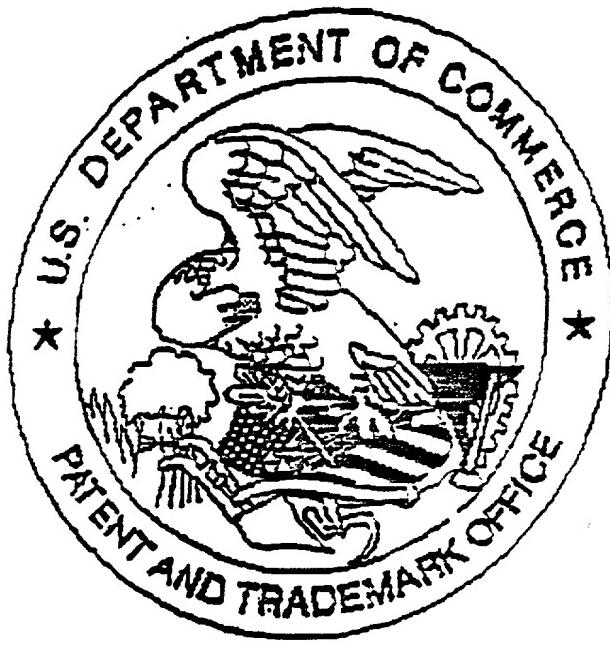
Additional Inventors are being named on separately numbered sheets attached hereto.

DECLARATION AND POWER OF ATTORNEY - Page 2

Docket No.: DM-6864-A

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